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(FILE 'HOME' ENTERED AT 09:25:38 ON 09 FEB 2004)  
SET COST OFF

FILE 'REGISTRY' ENTERED AT 09:26:33 ON 09 FEB 2004  
E METHYLENE CHLORIDE/CN

L1 1 S E3  
L2 15 S 189943-94-0 OR 153439-97-5 OR 146447-66-7 OR 142227-56-3 OR 1  
L3 448 S (C2H4O3 OR C4H4O4) AND (C3H6O3 OR C6H8O4)  
L4 26 S L3 AND 2/NC  
L5 11 S L4 NOT L2  
L6 4 S 10326-41-7 OR 79-33-4 OR 50-21-5 OR 26100-51-6  
L7 10 S 22098-76-6 OR 13076-19-2 OR 13076-17-0 OR 4511-42-6 OR 95-96-  
L8 5 S 26009-03-0 OR 502-97-6 OR 79-14-1 OR 26202-08-4 OR 26124-68-5  
E (C5H6O4)N/MF  
L9 13 S E3

FILE 'HCAPLUS' ENTERED AT 09:42:24 ON 09 FEB 2004

L10 23379 S L1  
L11 13139 S METHYLENE CHLORIDE OR METHYLENECHLORIDE  
L12 19 S METHANECHLORIDE OR METHANE CHLORIDE  
L13 19407 S DICHLOROMETHANE OR (DICHLORO OR DI CHLORO){}METHANE OR AEROTH  
L14 37830 S L10-L13  
L15 4318 S L2  
L16 57214 S L6,L7  
L17 136893 S LACTIC ACID OR LACTATE OR (POLYLACTIC OR POLY LACTIC){}ACID O  
L18 10124 S L8  
L19 18332 S GLYCOLIC ACID OR GLYCOLATE OR (POLYGLYCOLIC OR POLY GLYCOLIC)  
L20 7048 S L16,L17 AND L18,L19  
L21 274 S L15 AND L14  
L22 186 S L20 AND L14  
L23 318 S L21,L22  
L24 2273 S (POLYLACTIDE OR POLY(L) LACTIDE) AND (POLYGLYCOLIDE OR POLY(L)  
L25 8801 S (POLYLACTIDE OR POLY(L) LACTIDE OR L16,L17) AND (POLYGLYCOLIDE  
L26 283 S L14 AND L24,L25  
L27 323 S L23,L26  
L28 10266 S (?LACTIC? OR ?LACTIDE? OR ?LACTATE? OR L16 OR L17) AND (?GLYL  
L29 318 S L28 AND L14  
L30 329 S L27,L29  
L31 5 S L30 AND (ENDCAP? OR END CAP? OR UNCAP?)  
L32 97 S L30 AND CONTROL?(L) RELEAS?  
L33 82 S L30 AND (PY<=1995 OR PRY<=1995 OR AY<=1995)  
L34 1 S L33 AND L31  
L35 18 S L32 AND L33  
L36 19 S L34,L35  
E VANHAMONT J/AU  
L37 3 S E4,E5  
E VAN HAMONT J/AU  
L38 25 S E3-E8  
E REID R/AU  
L39 92 S E3,E15-E17  
E REID ROBERT/AU  
L40 76 S E1,E3,E16-E20  
E JACOB E/AU  
L41 81 S E3-E11  
L42 12 S E18,E19  
E JEYANTHI R/AU  
L43 22 S E3,E4  
E BOEDEKER E/AU  
L44 65 S E3,E4,E6,E7  
E MCQUEEN C/AU  
L45 22 S E3,E5,E10,E11

L46 E JARBOE D/AU  
 8 S E5,E6,E7  
 E CASSELS F/AU  
 L47 45 S E3-E9  
 E BROWN W/AU  
 L48 1836 S E3-E70  
 E BROWN WIL/AU  
 L49 5 S E12-E16  
 L50 1 S E22  
 L51 835 S BROWN WILLIAM?/AU  
 E THIES C/AU  
 L52 108 S E3-E5,E11  
 E TICE T/AU  
 L53 80 S E3,E4,E6-E9  
 E ROBERTS F/AU  
 L54 55 S E3,E8,E9  
 L55 11 S E44-E47,E29  
 L56 1 S E55  
 L57 1 S E67  
 L58 1 S E83  
 E FRIDEN P/AU  
 L59 62 S E3-E10  
 E SETTERSTROM J/AU  
 L60 30 S E3-E6  
 E SETTERSTROM J/AU  
 L61 4 S L30 AND L37-L60  
 L62 29 S L33 AND ?ENCAPSUL?  
 E DRUG DELIVERY/CT  
 L63 49 S L33 AND L18,L19,L22  
 L64 4 S L33 AND E27-E31  
 L65 0 S L33 AND E39,E43  
 L66 0 S L33 AND E49,E53,E55,E58  
 L67 1 S L33 AND E61,E64,E65,E70,E71  
 L68 0 S L33 AND E83,E84  
 L69 0 S L33 AND E89  
 L70 1 S L33 AND E97,E107,E108  
 L71 1 S L33 AND E112,E113,E115,E116  
 L72 0 S L33 AND E123,E128  
 L73 0 S L33 AND E136,E137,E139,E140  
 L74 0 S L33 AND E148,E150  
 L75 1 S L33 AND E162  
 L76 1 S L33 AND E182,E187,E188  
 L77 0 S L33 AND E195,E196,E199,E200,E201,E203  
 L78 0 S L33 AND E209,E211,E212  
 E PHARMACEUTICAL DOSAGE FORM/CT  
 L79 0 S L33 AND E11,E12,E18,E21  
 L80 9 S L33 AND E26,E27,E36  
 L81 1 S L33 AND E40,E46,E47  
 L82 0 S L33 AND E51,E53,E56,E59  
 L83 1 S L33 AND E62,E63,E68,E69  
 L84 0 S L33 AND E81  
 L85 0 S L33 AND E83,E87,E96  
 L86 5 S L33 AND E105,E106  
 L87 9 S L33 AND E110,E111,E113,E114  
 L88 0 S L33 AND E121,E131,E132  
 L89 0 S L33 AND E134,E135,E136,E144  
 L90 1 S L33 AND E146  
 L91 4 S L33 AND E158  
 L92 0 S L33 AND E179  
 L93 9 S L33 AND E184,E185,E192  
 L94 0 S L33 AND E193,E196,E197,E198,E200  
 L95 0 S L33 AND E206,E208,E209  
 L96 26 S L67-L95

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L97      30 S L36,L96
L98      220 S CFA() (1 OR I)
L99      0 S L33 AND L98
L100     135 S (COLONIZ? OR COLONIS?) ( ) FACTOR ( ) ANTIGEN? ( ) (I OR I)
L101     0 S L100 AND L33
L102     1 S COLI AND L33
L103     1 S (ESCHER? OR "E") ( ) COLI AND L33
L104     1 S L102,L103 AND L97
L105     7 S L33 AND (VACCIN? OR ADJUVANT?)
L106     3 S L97 AND L105
L107     6 S L64,L104,L106
L108     4 S L105 NOT L107
L109     10 S L107,L108
L110     24 S L97 NOT L109
L111     1 S L110 AND (VACCIN? OR ADJUVANT? OR IMMUNIZ? OR IMMUNIS?)
L112     11 S L109,L111
L113     23 S L110 NOT L112

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FILE 'HCAPLUS' ENTERED AT 10:41:32 ON 09 FEB 2004

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L114     11 S L112 AND L10-L113
L115     23 S L113 AND L10-L114

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=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 10:43:18 ON 09 FEB 2004

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

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FILE COVERS 1907 - 9 Feb 2004 VOL 140 ISS 7

FILE LAST UPDATED: 8 Feb 2004 (20040208/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L114 ANSWER 1 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:566792 HCAPLUS
DN 131:175064
ED Entered STN: 09 Sep 1999
TI Release-controlled hormone microsphere injection and
its preparation
IN Zhang, Wenchuan; Cheng, Lingmei; Zheng, Zhaohui; Xue, Qing
PA Chengdu Institute of Organic Chemistry, Chinese Academy of Sciences, Peop.
Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 6 pp.
CODEN: CNXXEV
DT Patent
LA Chinese
IC ICM A61K009-56
ICS A61J003-00

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CC 63-6 (Pharmaceuticals)  
Section cross-reference(s): 1, 2

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CN 1127634	A	19960731	CN 1995-111307	19950406 <--
PRAI	CN 1995-111307		19950406 <--		

AB The title injection comprises **release-controlled** hormone microspheres and antimicrobial solns. The microsphere **encapsulation** materials are bio-medical materials selected from e.g. biodegradable **polylactic acid**, **polyglycolic acid**, ethylene glycol-**glycolic acid** copolymer, polyamino acids, gelatine, and gum arabic. The hormones are estradiol valerate, estriol, testosterone propionate and T4 or T3. The weight of the **release-controlled** hormone microspheres is 5.0-50.0 mg, the **releasing** time in vitro is 30-90 days and the antimicrobial solns. contain 0.1-5% silicone oil II and 0.1-5% emulsifying agent in 0.9% normal saline; HLB of the emulsifying agent is 14-15.5. The average mol. weight of biodegradable materials is 3.0-10.0 x 104 and rate of the **microencapsulated** hormone is 2-20% of the weight of the microspheres. The outer surface of the microspheres is coated with beeswax. The organic phase for **encapsulating** microspheres are **methylene chloride**, chloroform, Et acetate, dioxane, Et ether, methylene and chloride-vegetable oil or chloroform-acetone; the emulsifying agent adopted by organic phase has HLB = 4.5-6 ; the aqueous phase contains PVA, PVP or PMANA aqueous solution The solvents for dissolving

beeswax

are chloroform, Et ether and vegetable oil. Hormone microspheres are sterilized by the ethylene oxide method at 30-45° for 48 h. The microspheres are suspended in antimicrobial solns. to form injections for i.m. administration.

ST **release controlled** hormone microsphere injection

IT **Drug delivery systems**  
(**controlled-release**; **release-controlled** hormone microsphere injection and its preparation)

IT **Drug delivery systems**  
(injections, **controlled-release** microsphere; **release-controlled** hormone microsphere injection and its preparation)

IT **Drug delivery systems**  
(injections, i.m., **controlled-release** microsphere; **release-controlled** hormone microsphere injection and its preparation)

IT **Drug delivery systems**  
(microspheres, in **controlled-release** injections; **release-controlled** hormone microsphere injection and its preparation)

IT Amino acids, biological studies  
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(polymers; **release-controlled** hormone microsphere injection and its preparation)

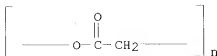
IT Beeswax  
Emulsifying agents  
(**release-controlled** hormone microsphere injection and its preparation)

IT Gelatins, biological studies  
Hormones, animal, biological studies  
Polysiloxanes, biological studies  
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(**release-controlled** hormone microsphere injection

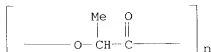
- and its preparation)
- IT Fats and Glyceridic oils, biological studies  
 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (vegetable; **release-controlled** hormone microsphere injection and its preparation)
- IT 50-27-1, Estriol 51-48-9, T4, biological studies 55-06-1, Sodium Triiodothyronine 57-85-2, Testosterone propionate 60-29-7, Ethyl ether, biological studies 67-64-1, 2-Propanone, biological studies 67-66-3, Chloroform, biological studies **75-09-2**, biological studies 75-21-8, Oxirane, biological studies 123-91-1, 1,4-Dioxane, biological studies 141-78-6, Acetic acid ethyl ester, biological studies 199-32-8, Estradiol valerate 2465-56-7, Methylene 6893-02-3, Triiodothyronine 9000-01-5, Gum arabic 9002-89-5, Poly (vinyl alcohol) 9003-39-8, Polyvinylpyrrolidone **26009-03-0**, **Polyglycolic acid 26023-30-3**, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] **26100-51-6**, **Polylactic acid 26124-68-5**, **Polyglycolic acid 34346-01-5**, Hydroxyacetic acid-lactic acid copolymer 54193-36-1, Sodium polymethacrylate 87430-88-4 122933-99-7  
 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (**release-controlled** hormone microsphere injection and its preparation)
- IT **75-09-2**, biological studies **26009-03-0**, **Polyglycolic acid 26023-30-3**, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] **26100-51-6**, **Polylactic acid 26124-68-5**, **Polyglycolic acid 34346-01-5**, Hydroxyacetic acid-lactic acid copolymer  
 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (**release-controlled** hormone microsphere injection and its preparation)
- RN 75-09-2 HCAPLUS  
 CN Methane, dichloro- (8CI, 9CI) (CA INDEX NAME)

Cl-CH<sub>2</sub>--Cl

- RN 26009-03-0 HCAPLUS  
 CN Poly[oxy(1-oxo-1,2-ethanediyl)] (9CI) (CA INDEX NAME)



- RN 26023-30-3 HCAPLUS  
 CN Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] (8CI, 9CI) (CA INDEX NAME)

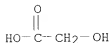


- RN 26100-51-6 HCAPLUS  
 CN Propanoic acid, 2-hydroxy-, homopolymer (9CI) (CA INDEX NAME)

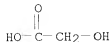
CM 1

CRN 50-21-5  
CMF C3 H6 O3RN 26124-68-5 HCAPLUS  
CN Acetic acid, hydroxy-, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 79-14-1  
CMF C2 H4 O3RN 34346-01-5 HCAPLUS  
CN Propanoic acid, 2-hydroxy-, polymer with hydroxyacetic acid (9CI) (CA INDEX NAME)

CM 1

CRN 79-14-1  
CMF C2 H4 O3

CM 2

CRN 50-21-5  
CMF C3 H6 O3

L114 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:120882 HCAPLUS  
Correction of: 1995:802867DN 130:129819  
Correction of: 123:237620

ED Entered STN: 24 Feb 1999

TI The preparation, characterization and pre-clinical evaluation of an orally administered HIV-1 **vaccine**, consisting of a branched peptide immunogen entrapped in **controlled release**

- microparticles
- AU O'Hagan, D. T.; McGee, J. P.; Boyle, R.; Gumaer, D.; Li, X.-M.; Potts, B.; Wang, C. Y.; Koff, W. C.
- CS United Biomedical, Inc., Hauppauge, NY, 11788, USA
- SO Journal of Controlled Release (1995), 36(1-2), 75-84  
CODEN: JCREEC; ISSN: 0168-3659
- PB Elsevier
- DT Journal
- LA English
- CC 63-3 (Pharmaceuticals)
- Section cross-reference(s): 15
- AB A **microencapsulated vaccine** was prepared, containing a branched peptide immunogen (200M), representing a portion of the principal neutralizing determinant of HIV-1, entrapped in **poly(lactide-co-glycolide)** microparticles. Following extensive in vitro characterization of the microparticles, which included assessments of particle size and size distributions, microparticle surface structure, antigen loading level and efficiency of entrapment, moisture content, the levels of residual solvent, the in vitro release rate, an assessment of antigen integrity, the product bioburden and stability during storage, the microparticles were assessed in vivo. The initial assessments undertaken, involved studies in different animal species to determine the safety and pyrogenicity of the **vaccine** and also the toxicity following oral administration. Once the microparticles had been shown to be safe, pyrogen free and non-toxic, they were assessed for their ability to induce serum IgG and neutralizing antibody responses in guinea pigs. Following oral immunization alone, and combined oral and s.c. immunization, the microparticles were shown to induce high levels of both serum IgG and neutralizing antibodies against HIV. Pending review by the U.S. Food and Drugs Administration, the microparticle based oral **vaccine** against HIV-1 will be assessed in clin. trials in seroneg. human volunteers.
- ST **controlled release microparticle oral vaccine**  
HIV1; branched peptide antigen microparticle oral **vaccine**
- IT Dissolution rate  
(antigen; preparation, characterization and pre-clin. evaluation of oral HIV-1 **vaccine** based on branched peptide immunogen entrapped in **controlled-release microparticles**)
- IT Peptides, biological studies  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(branched, preparation, characterization and pre-clin. evaluation of oral HIV-1 **vaccine** based on branched peptide immunogen entrapped in **controlled-release microparticles**)
- IT Animal virus  
(human immunodeficiency 1, preparation, characterization and pre-clin. evaluation of oral HIV-1 **vaccine** based on branched peptide immunogen entrapped in **controlled-release microparticles**)
- IT Polyesters, biological studies  
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(hydroxycarboxylic acid-based, preparation, characterization and pre-clin. evaluation of oral HIV-1 **vaccine** based on branched peptide immunogen entrapped in **controlled-release microparticles**)
- IT **Encapsulation**  
(micro-, preparation, characterization and pre-clin. evaluation of oral HIV-1 **vaccine** based on branched peptide immunogen entrapped in **controlled-release microparticles**)
- IT **Drug delivery systems**  
(microparticles, controlled-release,

preparation, characterization and pre-clin. evaluation of oral HIV-1  
**vaccine** based on branched peptide immunogen entrapped in  
**controlled-release** microparticles)

IT Antibodies  
 RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL  
 (Biological study); FORM (Formation, nonpreparative)  
 (neutralizing, preparation, characterization and pre-clin. evaluation of  
 oral HIV-1 **vaccine** based on branched peptide immunogen  
 entrapped in **controlled-release** microparticles)

IT **Vaccines**  
 (oral, preparation, characterization and pre-clin. evaluation of oral HIV-1  
**vaccine** based on branched peptide immunogen entrapped in  
**controlled-release** microparticles)

IT Particle size  
 Pyrogens  
 Safety  
 Toxicity  
 (preparation, characterization and pre-clin. evaluation of oral HIV-1  
**vaccine** based on branched peptide immunogen entrapped in  
**controlled-release** microparticles)

IT Antigens  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); PEP (Physical, engineering or chemical process); THU  
 (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (preparation, characterization and pre-clin. evaluation of oral HIV-1  
**vaccine** based on branched peptide immunogen entrapped in  
**controlled-release** microparticles)

IT AIDS (disease)  
 (preparation, characterization and pre-clin. evaluation of oral HIV-1  
**vaccine** in relation to AIDS)

IT 26780-50-7, Poly(DL-lactide-co-  
 glycolide)  
 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic  
 use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (preparation, characterization and pre-clin. evaluation of oral HIV-1  
**vaccine** based on branched peptide immunogen entrapped in  
**controlled-release** microparticles)

IT 75-09-2, Dichloromethane, uses  
 RL: NUU (Other use, unclassified); USES (Uses)  
 (solvent; preparation, characterization and pre-clin. evaluation of oral  
 HIV-1 **vaccine** based on branched peptide immunogen entrapped  
 in **controlled-release** microparticles)

IT 26780-50-7, Poly(DL-lactide-co-  
 glycolide)  
 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic  
 use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (preparation, characterization and pre-clin. evaluation of oral HIV-1  
**vaccine** based on branched peptide immunogen entrapped in  
**controlled-release** microparticles)

RN 26780-50-7 HCAPLUS  
 CN 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 1,4-dioxane-2,5-dione  
 (9CI) (CA INDEX NAME)

CM 1

CRN 502-97-6  
 CMF C4 H4 O4

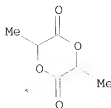




CM 2

CRN 95-96-5

CMF C6 H8 O4



IT 75-09-2, Dichloromethane, uses

RL: NUU (Other use, unclassified); USES (Uses)

(solvent; preparation, characterization and pre-clin. evaluation of oral HIV-1 vaccine based on branched peptide immunogen entrapped in **controlled-release** microparticles)

RN 75-09-2 HCAPLUS

CN Methane, dichloro- (8CI, 9CI) (CA INDEX NAME)

Cl-CH<sub>2</sub>-Cl

L114 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:78937 HCAPLUS

DN 130:100654

ED Entered STN: 08 Feb 1999

TI Preparation of polypeptide-type protein drug microspheres

IN Zhu, Kangjie; Jiang, Hongliang

PA Zhejiang Univ., Peop. Rep. China

SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 6 pp.

CODEN: CNXXEV

DT Patent

LA Chinese

IC ICM A61K009-56

CC 63-6 (Pharmaceuticals)

FAN.CNT 1

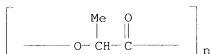
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CN 1122690	A	19960522	CN 1995-107205	19950609 <--
	CN 1069827	B	20010822		
PRAI	CN 1995-107205		19950609 <--		

AB Polypeptide-type protein drug microspheres are prepared by agitating an internal phase [glycerin-water and drugs] at 1000-4000 rpm and emulsifying a middle oil phase [**polylactic acid** or poly(**lactide-co- diglycolide**)] in acetone-**dichloromethane** (or chloroform)mixture ] to form W/O emulsion, agitating W/O emulsion at 400-1200 rpm and emulsifying in external water phase [PVA water solution with hydrolysis degree > 90% and concentration 0.5-10%.],

- vaporizing the solvent of the middle oil phase in W/O emulsion at 5-40°, microsphere hardening, centrifugal-separating, washing and vacuum drying. The polypeptide-type protein drug is hormone, enzyme, growth factor, Ig, polypeptide **vaccine**, cyclosporin, cytochrome, interferon or lymphokine.
- ST polypeptide protein drug microsphere
- IT Polymers, biological studies
- RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(co-, **lactide-diglycolide**; preparation of polypeptide-type protein drug microspheres)
- IT Proteins, general, biological studies
- RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(drugs; preparation of polypeptide-type protein drug microspheres)
- IT Drug delivery systems  
(microspheres; preparation of polypeptide-type protein drug microspheres)
- IT **Vaccines**  
(polypeptide; preparation of polypeptide-type protein drug microspheres)
- IT Cytochromes  
Enzymes, biological studies  
Growth factors, animal  
Hormones, animal, biological studies  
Immunoglobulins  
Interferons  
Lymphokines  
Myoglobins  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(preparation of polypeptide-type protein drug microspheres)
- IT Albumins, biological studies
- RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(serum, bovine; preparation of polypeptide-type protein drug microspheres)
- IT 9002-61-3, Chorionic gonadotropin
- RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(human; preparation of polypeptide-type protein drug microspheres)
- IT 56-81-5, Glycerin, biological studies 67-64-1, Acetone, biological studies 67-66-3, Chloroform, biological studies **75-09-2, Dichloromethane**, biological studies 9002-89-5, PVA 9003-20-7, PVA **26023-30-3**, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)]  
**26100-51-6, Polylactic acid** 79217-60-0, Cyclosporin  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(preparation of polypeptide-type protein drug microspheres)
- IT **75-09-2, Dichloromethane**, biological studies  
**26023-30-3**, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)]  
**26100-51-6, Polylactic acid**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(preparation of polypeptide-type protein drug microspheres)
- RN 75-09-2 HCAPLUS
- CN Methane, dichloro- (8CI, 9CI) (CA INDEX NAME)

Cl-CH<sub>2</sub>-Cl

RN 26023-30-3 HCAPLUS  
CN Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] (8CI, 9CI) (CA INDEX NAME)



RN 26100-51-6 HCAPLUS  
 CN Propanoic acid, 2-hydroxy-, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 50-21-5  
 CMF C3 H6 O3



L114 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN.  
 AN 1998:527193 HCAPLUS  
 DN 129:166193  
 ED Entered STN: 21 Aug 1998  
 TI Therapeutic treatment and prevention of infections with a bioactive material **encapsulated** within a biodegradable-biocompatible polymeric matrix  
 IN Setterstrom, Jean A.; Van Hamont, John E.; Reid, Robert H.; Jacob, Elliot; Jeyanthi, Ramasubbu; Boedeker, Edgar C.; McQueen, Charles E.; Tice, Thomas R.; Roberts, F. Donald; Friden, Phil  
 PA United States Dept. of the Army, USA; Van Hamont, John E.; et al.  
 SO PCT Int. Appl., 363 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K009-52  
 ICS A61K047-30  
 CC 63-5 (Pharmaceuticals)  
 Section cross-reference(s): 1, 2, 15  
 FAN.CNT 15

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9832427	A1	19980730	WO 1998-US1556	19980127
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	US 6309669	B1	20011030	US 1997-789734	19970127 <--
	AU 9863175	A1	19980818	AU 1998-63175	19980127
PRAI	US 1997-789734	A	19970127		
	US 1984-590308	B1	19840316	<--	
	US 1992-867301	A2	19920410	<--	
	US 1995-446148	A2	19950522	<--	
	US 1995-446149	B2	19950522	<--	
	US 1996-590973	B2	19960124		
	WO 1998-US1556	W	19980127		
AB	Novel burst-free, sustained release biocompatible and biodegradable microcapsules are disclosed which can be programmed to release their active core for variable durations ranging from 1-100 days in an aqueous physiolo. environment. The microcapsules are comprised of a core of polypeptide or other biol. active agent <b>encapsulated</b> in a matrix of <b>poly(lactide/glycolide)</b> copolymer, which may contain a pharmaceutically acceptable <b>adjuvant</b> , as a blend				

of uncapped free carboxyl end group and **end-capped** forms ranging in ratios from 100/0 to 1/99.

- ST infection microcapsule sustained release peptide copolymer
- IT Hepatitis  
(B, chronic; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Hepatitis  
(C, chronic; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Trypanosoma cruzi  
(Chagas' disease from; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Immunoglobulins  
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)  
(G, ampicillin-specific; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Nervous system  
(Huntington's chorea; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Antitumor agents  
(Kaposi's sarcoma; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Sperm  
(acrosome, proteinase of; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Diagnosis  
(agents; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Ragweed (Ambrosia)  
(allergy; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Ameba  
(amebiasis; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Antibiotics  
(aminoglycoside; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Absidia ramosa  
Actinobacillus equuli  
Actinobacillus seminis  
Arcanobacterium pyogenes  
Aspergillus fumigatus  
Babesia caballi  
Brucella melitensis  
Campylobacter fetus  
Campylobacter fetus intestinalis  
Candida albicans  
Candida tropicalis  
Chlamydia psittaci  
Clostridium tetani

Equid herpesvirus 1  
Equine arteritis virus

**Escherichia coli**

Gardnerella vaginalis  
Human herpesvirus 1  
Human herpesvirus 2  
Leptospira interrogans pomona  
Listeria monocytogenes  
Mycobacterium tuberculosis  
Mycoplasma bovigenitalium  
Mycoplasma hominis  
Neisseria gonorrhoeae  
Pneumocystis carinii  
Pseudomonas aeruginosa  
Rhodococcus equi  
Salmonella abortusovis  
Salmonella abortusovis  
Streptococcus group B  
Toxoplasma gondii  
Treponema pallidum  
Trichomonas vaginalis  
Trichomonas foetus  
Trypanosoma equiperdum

(antigens of; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)

- IT Mycobacterium  
(antimycobacterial agents; prevention of infections with bioactive  
material **encapsulated** within biodegradable-biocompatible  
polymeric matrix)
- IT Mouth  
(aphthous ulcer; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)
- IT Drugs  
(appetite stimulants; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)
- IT Heart, disease  
(arrhythmia; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)
- IT Blood vessel  
(artificial, infections surrounding; prevention of infections with  
bioactive material **encapsulated** within biodegradable-  
biocompatible polymeric matrix)
- IT Dermatitis  
(atopic; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)
- IT Babesia  
(babesiosis; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)
- IT Skin, neoplasm  
(basal cell carcinoma, inhibitors; prevention of infections with  
bioactive material **encapsulated** within biodegradable-  
biocompatible polymeric matrix)
- IT Antitumor agents  
Skin, neoplasm  
(basal cell carcinoma; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)

- IT Natural products, pharmaceutical  
RL: BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(belladonna; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Prostate gland  
(benign hyperplasia; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Polymers, biological studies  
RL: DEV (Device component use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(biodegradable; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Nervous system  
(central, disease; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Polymers, biological studies  
RL: BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(co-; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Intestine, disease  
(colitis; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Antigens  
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(colony factor; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Intestine, neoplasm  
(colorectal, inhibitors; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Antitumor agents  
Intestine, neoplasm  
(colorectal; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Thrombosis  
(coronary arterial; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Artery, disease  
(coronary, thrombosis; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Vasodilators  
(coronary; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Tapeworm (Cestoda)  
(cysticercosis; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)

- IT Bladder  
(cystitis; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)
- IT Mental disorder  
(depression; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)
- IT Eye, disease  
(diabetic retinopathy; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)
- IT Polyesters, biological studies  
RL: BPR (Biological process); BSU (Biological study, unclassified); DEV  
(Device component use); PRP (Properties); THU (Therapeutic use); BIOL  
(Biological study); PROC (Process); USES (Uses)  
(dilactone-based; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)
- IT Digestive tract  
(drugs for; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)
- IT Brain, disease  
(edema, peritumoral; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)
- IT Drug delivery systems  
(emulsions; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)
- IT B cell (lymphocyte)  
T cell (lymphocyte)  
(epitopes of; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)
- IT Alkaloids, biological studies  
RL: BPR (Biological process); BSU (Biological study, unclassified); DEV  
(Device component use); PRP (Properties); THU (Therapeutic use); BIOL  
(Biological study); PROC (Process); USES (Uses)  
(ergot; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)
- IT Amino acids, biological studies  
Fats and Glyceridic oils, biological studies  
RL: BPR (Biological process); BSU (Biological study, unclassified); DEV  
(Device component use); PRP (Properties); THU (Therapeutic use); BIOL  
(Biological study); PROC (Process); USES (Uses)  
(essential; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)
- IT Fasciola  
(fascioliasis; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)
- IT Filaria  
(filariasis; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)
- IT Anthelmintics  
(filaricides; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)

- IT Digestive tract  
(gastroenteritis, virus causing; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Intestine, disease  
(giardiasis; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Transplant and Transplantation  
(graft-vs.-host reaction; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Calymmatobacterium granulomatis  
(granuloma inguinale from, antigens of; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Antigens  
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(hepatitis B surface; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Liver, neoplasm  
(hepatoma, inhibitors; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Antitumor agents  
Liver, neoplasm  
(hepatoma; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Human herpesvirus 2  
(herpes genitalis from; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Human herpesvirus 3  
(herpes zoster from, antigens of; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Parvovirus  
Retroviridae  
(human; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Globulins, biological studies  
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(hyperimmune; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Sexual behavior  
(impotence; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Eye, disease  
Mouth  
Skin, disease  
(infection; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Prosthetic materials and Prosthetics  
(infections surrounding; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible



- polymeric matrix)
- IT Drug delivery systems  
(inhalants; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)
- IT Fertility  
Ovary, neoplasm  
Pancreas, neoplasm  
(inhibitors; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)
- IT Drug delivery systems  
(injections; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)
- IT Diabetes mellitus  
(insulin-dependent; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)
- IT Leishmania  
(leishmaniasis from, visceral; prevention of infections with bioactive  
material **encapsulated** within biodegradable-biocompatible  
polymeric matrix)
- IT Antitumor agents  
(lung small-cell carcinoma; prevention of infections with bioactive  
material **encapsulated** within biodegradable-biocompatible  
polymeric matrix)
- IT Antibiotics  
(macrolide; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)
- IT Antitumor agents  
(mammary gland; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)
- IT Antitumor agents  
(melanoma; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)
- IT Drug delivery systems  
(microcapsules; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)
- IT Drug delivery systems  
(microspheres; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)
- IT Drug delivery systems  
(nasal; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)
- IT Mammary gland  
Prostate gland  
(neoplasm, inhibitors; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)
- IT Mammary gland  
Prostate gland  
(neoplasm; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
matrix)
- IT Meningitis  
(neoplastic; prevention of infections with bioactive material

- encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Angiogenesis  
(neovascularization, retinal; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Diabetes mellitus  
(non-insulin-dependent; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Anti-inflammatory agents  
(nonsteroidal; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Emulsions  
(oil-in-water; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Drug delivery systems  
(oral; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Nitrites  
RL: BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(organic; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Antitumor agents  
(ovary; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Antitumor agents  
(pancreas; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Anxiety  
(panic disorder; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Paragonimus  
(paragonimiasis; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Hormones, animal, biological studies  
RL: BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(peptide; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Periodontium  
(periodontitis; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Mental disorder  
(phobia; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Adhesion, biological  
(postsurgical; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)

matrix)  
IT AIDS (disease)  
Acinetobacter  
Actinomycetales  
Adenoviridae  
Adrenoceptor agonists  
Aerococcus  
Aeromonas  
Allergy inhibitors  
Alzheimer's disease  
Analgesics  
Anesthetics  
Angiogenesis  
Angiogenesis inhibitors  
Anthelmintics  
Anti-infective agents  
Anti-inflammatory agents  
Antiarrhythmics  
Antiarthritics  
Antibacterial agents  
Antibiotics  
Anticholesteremic agents  
Anticoagulants  
Anticonvulsants  
Antidepressants  
Antidiabetic agents  
Antidiarrheals  
Antiemetics  
Antihistamines  
Antihypertensives  
Antimalarials  
Antimigraine agents  
Antiparkinsonian agents  
Antipyretics  
Antirheumatic agents  
Antiserums  
Antitumor agents  
Antitussives  
Antiulcer agents  
Antiviral agents  
Appetite depressants  
Arbovirus  
Arcanobacterium haemolyticum  
Arenavirus  
Asthma  
Bacillus (bacterium genus)  
Biocompatibility  
Blood substitutes  
Bordetella  
Borrelia  
Bronchodilators  
Brucella  
Cachexia  
Calymmatobacterium  
Campylobacter  
Cardiopulmonary bypass  
Cardiotonics  
Cardiovascular agents  
Cholinergic agonists  
Clostridium  
Contraceptives  
Coronavirus  
Corynebacterium

Cryptosporidium parvum  
Cystic fibrosis  
Cytomegalovirus  
Cytotoxic agents  
Decongestants  
Diagnosis  
Diarrhea  
Dissolution rate  
Diuretics  
Drug bioavailability  
Drug dependence  
Ebola virus  
Echinococcus  
Electrolytes, biological  
Emulsifying agents  
Enterobacteriaceae  
Enterococcus  
Enterovirus  
Epitopes  
Erysipelothrix  
Expectorants  
Filovirus  
Flavobacterium  
Freeze drying  
Fungicides  
Gardnerella  
Gram-negative bacteria  
Gram-positive bacteria (Firmicutes)  
Haemophilus  
Haemophilus ducreyi  
Helicobacter  
Hepatitis A virus  
Hepatitis B virus  
Hepatitis C virus  
Human herpesvirus 3  
Human herpesvirus 4  
Human immunodeficiency virus  
Human immunodeficiency virus 1  
Human parainfluenza virus  
Human poliovirus  
Hypercholesterolemia  
Hypnotics and Sedatives  
Immunization  
Immunomodulators  
Immunostimulants  
Infection  
Influenza virus  
Kidney, disease  
Lactococcus  
Legionella  
Leptospira  
Leuconostoc  
Listeria  
Measles virus  
Melanoma  
Micrococcus  
Molluscum contagiosum virus  
Moraxella  
Multiple sclerosis  
Mumps virus  
Muscle relaxants  
Narcotics  
Neisseria

Nervous system agents  
 Nutrients  
 Opioid antagonists  
 Osteoarthritis  
 Osteomyelitis  
 Osteoporosis  
 Ovary, neoplasm  
 Pancreas, neoplasm  
 Papillomavirus  
 Parasiticides  
 Parkinson's disease  
 Pediococcus  
 Planococcus (bacterium)  
 Plesiomonas  
 Pneumonia  
 Poxviridae  
 Pseudomonas  
 Psoriasis  
 Psychotropics  
 Rabies virus  
 Reoviridae  
 Respiratory syncytial virus  
 Rheumatoid arthritis  
 Rhinovirus  
 Rhodococcus  
 Rotavirus  
 Rothia (bacterium)  
 Rubella virus  
 Salmonella typhi  
 Sexually transmitted diseases  
 Shigella boydii  
 Shigella dysenteriae  
 Shigella flexneri  
 Shigella sonnei  
 Spirillum  
 Staphylococcus  
 Streptobacillus  
 Streptococcus  
 Thrombosis  
 Tranquilizers  
 Treponema

#### **Vaccines**

Vasodilators  
 Vibrio  
 Vibrio cholerae  
 Wolinella succinogenes  
 Yersinia

(prevention of infections with bioactive material **encapsulated**  
 within biodegradable-biocompatible polymeric matrix)

IT Alkaloids, biological studies  
 Antibodies  
 Antigens  
 Enzymes, biological studies  
 Estrogens  
 Glycolipids  
 Glycopeptides  
 Growth factors, animal  
 Lipopolysaccharides  
 Peptides, biological studies  
 Pheromones, animal  
 Progestogens  
 Prostaglandins  
 Proteins, general, biological studies

Steroids, biological studies

Sulfonamides

Tetracyclines

Vitamins

RL: BPR (Biological process); BSU (Biological study, unclassified); DEV

(Device component use); PRP (Properties); THU (Therapeutic use); BIOL

(Biological study); PROC (Process); USES (Uses)

(prevention of infections with bioactive material **encapsulated**  
within biodegradable-biocompatible polymeric matrix)

IT Drug delivery systems

(prodrugs; prevention of infections with bioactive material

**encapsulated** within biodegradable-biocompatible polymeric  
matrix)

IT Proliferation inhibition

(proliferation inhibitors; prevention of infections with bioactive  
material **encapsulated** within biodegradable-biocompatible  
polymeric matrix)

IT Antitumor agents

(prostate gland; prevention of infections with bioactive material

**encapsulated** within biodegradable-biocompatible polymeric  
matrix)

IT Pilus

(proteins; prevention of infections with bioactive material

**encapsulated** within biodegradable-biocompatible polymeric  
matrix)

IT Scalp

(psoriasis of; prevention of infections with bioactive material

**encapsulated** within biodegradable-biocompatible polymeric  
matrix)

IT Drug delivery systems

(rectal; prevention of infections with bioactive material

**encapsulated** within biodegradable-biocompatible polymeric  
matrix)

IT Artery, disease

(restenosis; prevention of infections with bioactive material

**encapsulated** within biodegradable-biocompatible polymeric  
matrix)

IT Eye, disease

(retina, neovascularization; prevention of infections with bioactive

material **encapsulated** within biodegradable-biocompatible  
polymeric matrix)

IT Schistosoma

(schistosomiasis from; prevention of infections with bioactive material

**encapsulated** within biodegradable-biocompatible polymeric  
matrix)

IT Lung, neoplasm

(small-cell carcinoma, inhibitors; prevention of infections with

bioactive material **encapsulated** within biodegradable-  
biocompatible polymeric matrix)

IT Lung, neoplasm

(small-cell carcinoma; prevention of infections with bioactive material

**encapsulated** within biodegradable-biocompatible polymeric  
matrix)

IT Muscle relaxants

(spasmolytics; prevention of infections with bioactive material

**encapsulated** within biodegradable-biocompatible polymeric  
matrix)

IT Contraceptives

(spermicidal; prevention of infections with bioactive material

**encapsulated** within biodegradable-biocompatible polymeric  
matrix)

IT Brain, disease

(spongiform encephalopathy, agent causing; prevention of infections

- with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Appetite  
(stimulants; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Brain, disease  
(stroke; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Strongylus  
(strongylodiasis; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Drug delivery systems  
(sustained-release, programmable; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Osteoporosis  
(therapeutic agents; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Bile  
(therapy with; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Drug delivery systems  
(topical; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Muscle, disease  
(torticollis, spasmodic; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Toxocara  
(toxocariasis; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Toxoplasma gondii  
(toxoplasmosis from; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Drug delivery systems  
(transdermal; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Head  
(trauma; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Trichinella  
(trichinellosis; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Trichomonas  
(trichomoniasis; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Drug delivery systems  
(vaginal; prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)
- IT Emulsions

- (water-in-oil; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
 matrix)
- IT Lactams  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 ( $\beta$ -, antibiotics; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
 matrix)
- IT 9002-72-6, Somatotropin  
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
 (deficiency; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
 matrix)
- IT 9005-49-6, Heparin, biological studies  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL  
 (Biological study); PROC (Process)  
 (neutralization of; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
 matrix)
- IT 9001-60-9, Lactate dehydrogenase 37326-33-3, Hyaluronidase  
 RL: BPR (Biological process); BSU (Biological study, unclassified); DEV  
 (Device component use); PRP (Properties); THU (Therapeutic use); BIOL  
 (Biological study); PROC (Process); USES (Uses)  
 (of sperm; prevention of infections with bioactive material  
**encapsulated** within biodegradable-biocompatible polymeric  
 matrix)
- IT 50-06-6, Phenobarbital, biological studies 50-12-4, Mephenytoin  
 50-18-0, Cyclophosphamide 50-23-7, Hydrocortisone 50-24-8,  
 Prednisolone 50-28-2, 17 $\beta$ -Estradiol, biological studies 50-33-9,  
 Phenylbutazone, biological studies 50-52-2, Thioridazine 50-55-5,  
 Reserpine 50-78-2, Aspirin 51-55-8, Atropine, biological studies  
 52-24-4, Thiotepa 52-76-6, Lynestrenol 53-03-2, Prednisone 53-16-7,  
 Estrone, biological studies 53-86-1, Indomethacin 54-11-5, Nicotine  
 55-48-1, Atropine sulfate 55-63-0, Nitroglycerin 55-86-7, Nitrogen  
 mustard 56-53-1, Diethyl stilbestrol 56-75-7, Chloramphenicol  
 57-27-2, Morphine, biological studies 57-33-0, Sodium pentobarbital  
 57-42-1, Meperidine 57-53-4, Meprobamate 57-63-6, Ethinyl estradiol  
 57-85-2, Testosterone propionate 57-92-1, Streptomycin a, biological  
 studies 58-08-2, Caffeine, biological studies 58-14-0, Pyrimethamine  
 58-22-0 58-25-3, Chlordiazepoxide 58-39-9, Perphenazine 58-73-1,  
 Diphenhydramine 59-01-8, Kanamycin a 59-05-2, Methotrexate 59-92-7,  
 L-Dopa, biological studies 61-33-6, Penicillin g, biological studies  
 67-20-9, Nitrofurantoin 68-22-4, Norethisterone 68-23-5, Norethynodrel  
 69-09-0, Chlorpromazine hydrochloride 69-53-4, Ampicillin 69-72-7D,  
 Salicylic acid, derivs. 71-58-9, Medroxyprogesterone acetate 72-33-3,  
 Mestranol 76-57-3, Codeine 79-57-2, Oxytetracycline 79-64-1,  
 Dimethisterone 91-81-6, Tripeleminamine 103-90-2, Acetaminophen  
 113-15-5, Ergotamine 114-07-8, Erythromycin 114-49-8, Hyoscine  
 hydrobromide 121-54-0 122-09-8, Phentermine 125-29-1,  
 Dihydrocodeinone 125-71-3, Dextromethorphan 127-48-0, Trimethadione  
 128-62-1, Noscapine 145-94-8, Chlorindanol 148-82-3, Melphalan  
 155-41-9, Methscopolamine bromide 288-32-4D, Imidazole, derivs.  
 297-76-7, Ethynodiol diacetate 302-22-7, Chloralminone acetate  
 305-03-3, Chlorambucil 309-43-3, Sodium secobarbital 315-30-0,  
 Allopurinol 434-03-7, Ethisterone 439-14-5, Diazepam 443-48-1,  
 Metronidazole 469-62-5 471-34-1, Calcium carbonate, biological studies  
 497-19-8, Sodium carbonate, biological studies 523-87-5, Dimenhydrinate  
 546-93-0, Magnesium carbonate 578-66-5D, 8-Aminoquinoline, derivs.  
 578-68-7D, 4-Aminoquinoline, derivs. 595-33-5, Megestrol acetate  
 738-70-5, Trimethoprim 846-50-4, Temazepam 1397-89-3, Amphoterin b  
 1397-94-0, Antimycin a 1403-66-3, Gentamicin 1404-26-8, Polymyxin b  
 1404-90-6, Vancomycin 1406-05-9D, Penicillin, derivs. 4696-76-8,  
 Kanamycin b 5588-33-0, Mesoridazine 5633-18-1, Melengestrol



5786-21-0, Clozapine 5800-19-1, Metiapine 6533-00-2, Norgestrel 7447-40-7, Potassium chloride (KCl), biological studies 8063-07-8, Kanamycin 9000-83-3, Atpase 9000-92-4, Amylase 9001-62-1, Lipase 9001-63-2, Muramidase 9001-67-6, Neuraminidase 9001-78-9, Alkaline phosphatase 9001-99-4, Ribonuclease 9002-02-2, Succinic acid dehydrogenase 9002-07-7, Trypsin 9004-07-3, Chymotrypsin 9004-10-8, Insulin, biological studies 9025-82-5, Phosphodiesterase 9029-12-3, Glutamic acid dehydrogenase 9035-74-9, Glycogen phosphorylase 9046-27-9,  $\gamma$ -Glutamyltranspeptidase 9079-67-8 10118-90-8, Minocycline 11111-12-9, Cephalosporins 13292-46-1, Rifampin 14271-04-6 21645-51-2, Aluminum hydroxide, biological studies 22232-71-9, Mazindol - 24730-10-7, Dihydroergocristine methanesulfonate 25447-66-9 **26780-50-7, Poly(lactide co-glycolide)** 26787-78-0, Amoxicillin 30516-87-1, Azt 32986-56-4, Tobramycin 35189-28-7, Norgestimate 37205-61-1, Proteinase inhibitor 37517-28-5, Amikacin 53678-77-6D, Muramyl dipeptide, derivs. 53994-73-3, Cefaclor 55268-75-2, Cefuroxime 61036-62-2, Teicoplanin 64221-86-9, Imipenem 80738-43-8, Lincosamide 81103-11-9, Clarithromycin 82419-36-1, Ofloxacin 85721-33-1, Ciprofloxacin

RL: BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)

IT 9002-60-2, Adrenocorticotropin, biological studies 9007-12-9, Calcitonin 9034-40-6, Lhrh 62229-50-9, Epidermal growth factor 115966-68-2, Histatin 5 (human parotid saliva) 123781-17-9, Histatin 127716-52-3, Histatin 9 (human parotid saliva) 146553-69-7 174270-18-9, 5-25-Histatin 6 (human parotid saliva) 186138-55-6 186138-60-3 194017-97-5 211118-03-5

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)

IT 9005-64-5, Tween 20 9005-65-6, Tween 80 9005-67-8, Tween 60 106392-12-5, Pluronic

RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)

IT 75-09-2, uses

RL: NUU (Other use, unclassified); USES (Uses)

(prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)

IT 146553-70-0 146553-71-1 146553-72-2 146553-73-3 146553-74-4 146553-75-5 146553-76-6 146553-77-7 146553-78-8 146553-81-3 146553-82-4 146553-83-5 146553-85-7 146553-86-8 146553-87-9 146553-88-0 146553-89-1 146553-90-4 146553-91-5 146553-92-6 164583-46-4 164583-50-0 164583-51-1 211118-14-8 211118-17-1

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(prevention of infections with bioactive material **encapsulated** within biodegradable-biocompatible polymeric matrix)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD  
RE

- (1) Jeyanthi; Proceedings International Symposium on Controlled Release of Bioactive Materials 1996, P351 HCAPLUS
- (2) Oppenheim; US 5486503 A 1996 HCAPLUS
- (3) Syntex U S A Inc; EP 0052510 B2 1994 HCAPLUS
- (4) Wang; J of Controlled Release 1991, V17, P23 HCAPLUS
- (5) Yan; J of Controlled Release 1994, V32(3), P231 HCAPLUS
- (6) Yeh; A Novel Emulsification-Solvent Extraction Technique for Production of

Protein Loaded Biodegradable Microparticles for Vaccine and Drug Delivery  
1995, V33(3), P437 HCAPLUS

IT 26780-50-7, Poly(lactide co-glycolide

)

RL: BPR (Biological process); BSU (Biological study, unclassified); DEV  
(Device component use); PRP (Properties); THU (Therapeutic use); BIOL  
(Biological study); PROC (Process); USES (Uses)  
(prevention of infections with bioactive material **encapsulated**  
within biodegradable-biocompatible polymeric matrix)

RN 26780-50-7 HCAPLUS

CN 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 1,4-dioxane-2,5-dione  
(9CI) (CA-INDEX NAME)

CM 1

CRN 502-97-6

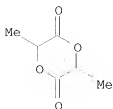
CMF C4 H4 O4



CM 2

CRN 95-96-5

CMF C6 H8 O4



IT 75-09-2, uses

RL: NUU (Other use, unclassified); USES (Uses)  
(prevention of infections with bioactive material **encapsulated**  
within biodegradable-biocompatible polymeric matrix)

RN 75-09-2 HCAPLUS

CN Methane, dichloro- (8CI, 9CI) (CA INDEX NAME)

Cl-CH2-Cl

L114 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:594553 HCAPLUS

DN 127:253185

ED Entered STN: 17 Sep 1997

TI **Controlled-release** compositions of hydroxamic acids

IN Kamei, Shigeru; Kamijo, Akiko; Igari, Yasutaka; Kato, Kaneyoshi

PA Takeda Chemical Industries, Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 33 pp.

CODEN: JKXXAF

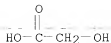
DT Patent  
 LA Japanese  
 IC ICM A61K031-16  
 ICS A61K009-52; A61K031-165; A61K047-34; C08G063-06; C07C259-06  
 CC 63-6 (Pharmaceuticals)  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 09221420	A2	19970826	JP 1996-328582	19961209 <--
PRAI	JP 1995-327676		19951215 <--		
AB	<b>Controlled-release</b> compns. comprise hydroxamic acids [e.g. 7-(4-methoxyphenyl)-7-(3-methyl-1,4-naphthoquinon-2-yl)heptanohydroxamic acid and 7,7-bis(4-methoxyphenyl)-7-cyanoheptanoxamic acid] or their salts and biodegradable carboxy group-containing polymers or their salts [such as <b>glycolic acid-lactic acid</b> copolymer iron salt]. <b>Glycolic acid-lactic acid</b> copolymer iron salt and 7-(4-methoxyphenyl)-7-(3-methyl-1,4-naphthoquinon-2-yl)heptanohydroxamic acid in <b>dichloromethane</b> were mixed with polyvinyl alc. and made into <b>slow-release</b> microcapsules.				
ST	<b>controlled release</b> compn hydroxamic acid				
IT	Polymers, biological studies RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (biodegradable carboxy group-containing; <b>controlled-release</b> compns. of hydroxamic acids)				
IT	Dissolution rate ( <b>controlled-release</b> compns. of hydroxamic acids)				
IT	Hydroxamic acids RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) ( <b>controlled-release</b> compns. of hydroxamic acids)				
IT	<b>Drug delivery systems</b> ( <b>controlled-release; controlled-release</b> compns. of hydroxamic acids)				
IT	Carboxylic acids, biological studies RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (hydroxy, polymers; <b>controlled-release</b> compns. of hydroxamic acids)				
IT	<b>Drug delivery systems</b> ( <b>microcapsules; controlled-release</b> compns. of hydroxamic acids)				
IT	<b>Drug delivery systems</b> <b>Drug delivery systems</b> (solns., injection, <b>slow-release; controlled-release</b> compns. of hydroxamic acids)				
IT	5470-11-1, Hydroxylamine hydrochloride		103185-95-1	103186-54-5	
	186523-31-9	195879-12-0			
	RL: RCT (Reactant); RACT (Reactant or reagent) ( <b>controlled-release</b> compns. of hydroxamic acids)				
IT	<b>34346-01-5P, Glycolic acid-lactic acid</b> copolymer				
	102012-38-4P	146845-98-9P	183965-50-6P		
	183965-51-7P	186502-53-4P	186522-67-8P	195879-09-5P	195879-10-8P
	195879-11-9P	195879-13-1P	195879-14-2P	195879-15-3P	
	RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) ( <b>controlled-release</b> compns. of hydroxamic acids)				
IT	<b>34346-01-5P, Glycolic acid-lactic acid</b> copolymer				
	RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) ( <b>controlled-release</b> compns. of hydroxamic acids)				
RN	34346-01-5	HCAPLUS			

CN Propanoic acid, 2-hydroxy-, polymer with hydroxyacetic acid (9CI) (CA  
INDEX NAME)

CM 1

CRN 79-14-1  
CMF C2 H4 O3



CM 2

CRN 50-21-5  
CMF C3 H6 O3



L114 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1996:761877 HCAPLUS

DN 126:37147

ED Entered STN: 01 Jan 1997

TI Implantable bioresorbable membrane and method for the preparation thereof

IN Yoon, Seok Joon; Yeo, Guw Dong; Kim, You Chan; Seo, Min Hyo; Pai, Chaul  
Min; Jung, Jong Pyoung; Lee, Seung Jin

PA Sam Yang Co. Ltd., S. Korea; Yoon, Seok Joon; Yeo, Guw Dong; Kim, You  
Chan; Seo, Min Hyo; Pai, Chaul Min; Jung, Jong Pyoung; Lee, Seung Jin

SO PCT Int. Appl., 26 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61L027-00

ICS A61F002-02; A61K009-00

CC 63-7 (Pharmaceuticals)

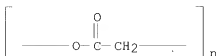
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9634634	A1	19961107	WO 1996-KR63	19960501 <--
	W: AT, CA, CH, CN, DE, DK, ES, GB, JP, KP, LU, NO, SE, US, VN				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2219995	AA	19961107	CA 1996-2219995	19960501 <--
	CN 1183051	A	19980527	CN 1996-193670	19960501 <--
	EP 857072	A1	19980812	EP 1996-912319	19960501 <--
	EP 857072	B1	20030115		
	R: DE, FR, GB, IT				
	JP 11504341	T2	19990420	JP 1996-533190	19960501 <--
PRAI	KR 1995-10672	A	19950501 <--		
	KR 1995-35025	A	19951012 <--		
	WO 1996-KR63	W	19960501		

AB An implantable bioresorbable membrane for the separation and regeneration of tissues in a defect site, which comprises a woven or knitted fabric made of bioresorbable fibers and a process bioresorbable/biocompatible polymer film coated thereon. The implantable bioresorbable membrane of the present invention is produced by preparing a fabric as a support from

- bioresorbable fibrous materials, coating the fabric with a solution containing
- a bioresorbable/biocompatible polymer and a pore forming agent, treating the coated fabric to generate pores, and embossing the coated fabric. A membrane was prepared from **polyglycolic acid** multifilament and poly(L-lactic acid) and polyd(L-lactic acid-glycolic acid) coating.
- ST implant bioresorbable membrane polyester
- IT Growth factors, animal  
RL: MOA (Modifier or additive use); POF (Polymer in formulation); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(epithelial cell growth factors; implantable bioresorbable membrane)
- IT Anti-inflammatory agents  
(implantable bioresorbable membrane)
- IT Platelet-derived growth factors  
RL: MOA (Modifier or additive use); POF (Polymer in formulation); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(implantable bioresorbable membrane)
- IT Polyester fibers, biological studies  
RL: PEP (Physical, engineering or chemical process); POF (Polymer in formulation); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(implantable bioresorbable membrane)
- IT Polyesters, biological studies  
RL: PEP (Physical, engineering or chemical process); POF (Polymer in formulation); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(implantable bioresorbable membrane)
- IT Growth factors, animal  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(implantable bioresorbable membrane)
- IT **Drug delivery systems**  
**Drug delivery systems**  
(implants, controlled-release;  
implantable bioresorbable membrane)
- IT Prosthetic materials and Prosthetics  
(implants; implantable bioresorbable membrane)
- IT Proteins, specific or class  
RL: MOA (Modifier or additive use); POF (Polymer in formulation); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(morphogenetic; implantable bioresorbable membrane)
- IT Medical goods  
(sutures; implantable bioresorbable membrane)
- IT **26009-03-0, Polyglycolic acid**  
**26124-68-5, Polyglycolic acid**  
RL: PEP (Physical, engineering or chemical process); POF (Polymer in formulation); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(fibers; implantable bioresorbable membrane)
- IT 53-86-1, Indomethacin 57-48-7, D-Fructose, biological studies 60-54-8, Tetracycline 61-68-7, Mefenamic acid 69-79-4, Maltose 79-57-2, Oxytetracycline 144-55-8, Sodium bicarbonate, biological studies 443-48-1, Metronidazole 497-19-8, Sodium carbonate, biological studies 994-36-5, Sodium citrate 5104-49-4, Flurbiprofen 7447-40-7, Potassium chloride, biological studies 7647-14-5, Sodium chloride (NaCl), biological studies 9000-07-1, Carrageenan 9000-69-5, Pectin 9003-39-8, Pvp 9004-54-0, Dextran, biological studies 9005-32-7, Alginic acid 9014-63-5, Xylan 10043-52-4, Calcium chloride, biological studies 10118-90-8, Minocycline 12125-02-9, Ammonium chloride, biological studies 15687-27-1, Ibuprofen 22204-53-1, Naproxen 61912-98-9, Insulin-like growth factor  
RL: MOA (Modifier or additive use); POF (Polymer in formulation); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

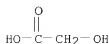
- (implantable bioresorbable membrane)
- IT 64-17-5, Ethanol, uses **75-09-2, Methylene chloride**, uses 141-78-6, Ethyl acetate, uses 872-50-4, N-Methylpyrrolidone, uses  
 RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); PROC (Process); USES (Uses)  
 (implantable bioresorbable membrane)
- IT 24980-41-4, Polycaprolactone 25248-42-4, Polycaprolactone  
**26161-42-2**, 26811-96-1, Poly(L-lactic acid)  
 29223-92-5, Poly-p-dioxanone 31621-87-1, Poly-p-dioxanone SRU  
 31852-84-3, Poly(trimethylene carbonate) 50862-75-4, Poly(oxycarbonyloxy-1,3-propanediyl) **54512-07-1, Glycolic acid**  
 -L-lactic acid copolymer  
 RL: PEP (Physical, engineering or chemical process); POF (Polymer in formulation); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (implantable bioresorbable membrane)
- IT **26009-03-0, Polyglycolic acid**  
**26124-68-5, Polyglycolic acid**  
 RL: PEP (Physical, engineering or chemical process); POF (Polymer in formulation); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (fibers; implantable bioresorbable membrane)
- RN 26009-03-0 HCAPLUS  
 CN Poly[oxy(1-oxo-1,2-ethanediyl)] (9CI) (CA INDEX NAME)



- RN 26124-68-5 HCAPLUS  
 CN Acetic acid, hydroxy-, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 79-14-1  
 CMF C2 H4 O3



- IT **75-09-2, Methylene chloride**, uses  
 RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); PROC (Process); USES (Uses)  
 (implantable bioresorbable membrane)
- RN 75-09-2 HCAPLUS  
 CN Methane, dichloro- (8CI, 9CI) (CA INDEX NAME)

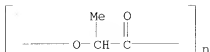
Cl-CH<sub>2</sub>-Cl

- IT **26161-42-2 54512-07-1, Glycolic acid**  
 -L-lactic acid copolymer  
 RL: PEP (Physical, engineering or chemical process); POF (Polymer in formulation); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(implantable bioresorbable membrane)

RN 26161-42-2 HCAPLUS

CN Poly[oxy(1S)-1-methyl-2-oxo-1,2-ethanediyl]] (9CI) (CA INDEX NAME)



RN 54512-07-1 HCAPLUS

CN Propanoic acid, 2-hydroxy-, (2S)-, polymer with hydroxyacetic acid (9CI)  
(CA INDEX NAME)

CM 1

CRN 79-33-4

CMF C3 H6 O3

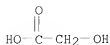
Absolute stereochemistry. Rotation (+).



CM 2

CRN 79-14-1

CMF C2 H4 O3



L114 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:999165 HCAPLUS

DN 124:66330

ED Entered STN: 22 Dec 1995

TI Enhancement of protective immune responses to Venezuelan equine encephalitis (VEE) virus with **microencapsulated vaccine**

AU Greenway, Terrence E.; Eldridge, John H.; Ludwig, George; Staas, Jay K.; Smith, Jonathan F.; Gilley, Richard M.; Michalek, Suzanne M.

CS Department of Microbiology, University of Alabama, Birmingham, AL, 35294, USA

SO Vaccine (1995), 13(15), 1411-20

CODEN: VACCDE; ISSN: 0264-410X

PB Elsevier

DT Journal

LA English

CC 63-3 (Pharmaceuticals)

Section cross-reference(s): 15

AB Venezuelan equine encephalomyelitis (VEE) virus is a mosquito-borne arbovirus of major human health significance in the New World. Currently two forms of VEE virus are used for immunization of humans and horses, i.e. a live attenuated and a formalin-inactivated **vaccine**. Clin. evidence suggests that these **vaccines** are not fully

efficacious and may produce certain undesirable side-effects. In the present study, microspheres composed of biocompatible and biodegradable poly (DL-lactide-co-glycolide) (DL-PLG) were evaluated for their effectiveness as a delivery system of whole, inactivated VEE virus **vaccine** for the induction of protective immune responses. Mice receiving 50 µg VEE virus in microspheres composed of an equimolar ratio of DL-lactide and glycolide (50:50 DL-PLG) exhibited a primary circulating IgG antibody response which was approx. 32-times higher than the response induced with the same dose of **unencapsulated** (free) virus. A similar difference in responses was seen with antigen doses ranging from 3.1 to 50 µg. A rapid increase in antibody activity was seen after the secondary immunization (day 50). Formalin fixation of inactivated VEE virus was important for immunogenicity since the circulating anti-VEE virus antibody response induced with **microencapsulated** nonformalin-fixed virus **vaccine** was lower than that induced with **microencapsulated** formalin fixed virus **vaccine**. Furthermore, at low antigen concns., DL-PLG microsphere **vaccines** prepared with the solvent **methylene chloride** induced higher antibody responses than those prepared using Et acetate as the solvent. **Microencapsulated vaccine** also induced higher VEE virus neutralization titers than did free virus **vaccine**. Finally, the **microencapsulated** virus was more effective than the free virus in inducing immune responses protective against systemic challenge with virulent VEE virus. These results demonstrate that DL-PLG microspheres containing formalin-fixed, inactivated VEE virus were effective in augmenting circulating IgG antibody levels and neutralization titers to the VEE virus following systemic immunization and in affording enhanced protection against systemic challenge with virulent VEE virus. The effects of antigen form and the microsphere processing solvent on the immunogenicity of the **vaccine** are discussed.

ST immune response equine encephalitis virus **microencapsulation**

IT **Vaccines**

(immune responses to Venezuelan equine encephalitis virus with **microencapsulated vaccine**)

IT Immunoglobulins

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)

(G, immune responses to Venezuelan equine encephalitis virus with **microencapsulated vaccine**)

IT Virus, animal

(Venezuelan equine encephalomyelitis, immune responses to Venezuelan equine encephalitis virus with **microencapsulated vaccine**)

IT Pharmaceutical dosage forms

(microspheres, immune responses to Venezuelan equine encephalitis virus with **microencapsulated vaccine**)

IT 26780-50-7

RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(immune responses to Venezuelan equine encephalitis virus with **microencapsulated vaccine**)

IT 26780-50-7

RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(immune responses to Venezuelan equine encephalitis virus with **microencapsulated vaccine**)

RN 26780-50-7 HCAPIUS

CN 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 1,4-dioxane-2,5-dione (9CI) (CA INDEX NAME)

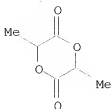


CRN 502-97-6  
CMF C4 H4 O4



CM 2

CRN 95-96-5  
CMF C6 H8 O4



L114 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:802867 HCAPLUS

DN 123:237620

ED Entered STN: 20 Sep 1995

TI The preparation, characterization and pre-clinical evaluation of an orally administered HIV-1 **vaccine**, consisting of a branched peptide immunogen entrapped in **controlled release** microparticles

AU O'Hagan, D. T.; P McGee, J.; Boyle, R.; Gumaer, D.; Li, X.-M.; Potts, B.; Wang, C. Y.; Koff, W. C.

CS United Biomedical, Inc., Hauppauge, NY, 11788, USA

SO Journal of Controlled Release (1995), 36(1-2), 75-84

CODEN: JCREEC; ISSN: 0168-3659

PB Elsevier

DT Journal

LA English

CC 63-3 (Pharmaceuticals)

Section cross-reference(s): 15

AB A **microencapsulated vaccine** was prepared, containing a branched peptide immunogen (200M), representing a portion of the principal neutralizing determinant of HIV-1, entrapped in **poly(lactide-co-glycolide)** microparticles. Following extensive in vitro characterization of the microparticles, which included assessments of particle size and size distributions, microparticle surface structure, antigen loading level and efficiency of entrapment, moisture content, the levels of residual solvent, the in vitro release rate, an assessment of antigen integrity, the product bioburden and stability during storage, the microparticles were assessed in vivo. The initial assessments undertaken, involved studies in different animal species to determine the safety and pyrogenicity of the **vaccine** and also the toxicity following oral administration. Once the microparticles had been shown to be safe, pyrogen free and non-toxic, they were assessed for their ability to induce serum IgG and neutralizing antibody responses in guinea pigs. Following oral immunization alone, and combined oral and s.c.

immunization, the microparticles were shown to induce high levels of both serum IgG and neutralizing antibodies against HIV. Pending review by the U.S. Food and Drugs Administration, the microparticle based oral **vaccine** against HIV-1 will be assessed in clin. trials in seroneg. human volunteers.

- ST **controlled release microparticle oral vaccine**  
 IT HIV1; branched peptide antigen microparticle oral **vaccine**  
 IT Solution rate  
     (antigen; preparation, characterization and pre-clin. evaluation of oral HIV-1 **vaccine** based on branched peptide immunogen entrapped in **controlled-release** microparticles)  
 IT Particle size  
     Pyrogens  
     Safety  
     Toxicity  
         (preparation, characterization and pre-clin. evaluation of oral HIV-1 **vaccine** based on branched peptide immunogen entrapped in **controlled-release** microparticles)  
 IT Antigens  
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
         (preparation, characterization and pre-clin. evaluation of oral HIV-1 **vaccine** based on branched peptide immunogen entrapped in **controlled-release** microparticles)  
 IT Acquired immune deficiency syndrome  
     (preparation, characterization and pre-clin. evaluation of oral HIV-1 **vaccine** in relation to AIDS)  
 IT Peptides, biological studies  
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
         (branched, preparation, characterization and pre-clin. evaluation of oral HIV-1 **vaccine** based on branched peptide immunogen entrapped in **controlled-release** microparticles)  
 IT Virus, animal  
     (human immunodeficiency 1, preparation, characterization and pre-clin. evaluation of oral HIV-1 **vaccine** based on branched peptide immunogen entrapped in **controlled-release** microparticles)  
 IT Polyesters, biological studies  
     RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
         (hydroxycarboxylic acid-based, preparation, characterization and pre-clin. evaluation of oral HIV-1 **vaccine** based on branched peptide immunogen entrapped in **controlled-release** microparticles)  
 IT Encapsulation  
     (micro-, preparation, characterization and pre-clin. evaluation of oral HIV-1 **vaccine** based on branched peptide immunogen entrapped in **controlled-release** microparticles)  
 IT Pharmaceutical dosage forms  
     (microparticles, **controlled-release**, preparation, characterization and pre-clin. evaluation of oral HIV-1 **vaccine** based on branched peptide immunogen entrapped in **controlled-release** microparticles)  
 IT Antibodies  
     RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)  
         (neutralizing, preparation, characterization and pre-clin. evaluation of oral HIV-1 **vaccine** based on branched peptide immunogen entrapped in **controlled-release** microparticles)  
 IT Vaccines

(oral, preparation, characterization and pre-clin. evaluation of oral HIV-1 vaccine based on branched peptide immunogen entrapped in **controlled-release** microparticles)

IT 26780-50-7, Poly(DL-lactide-co-glycolide)

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(preparation, characterization and pre-clin. evaluation of oral HIV-1 vaccine based on branched peptide immunogen entrapped in **controlled-release** microparticles)

IT 75-09-2, Dichloromethane, uses

RL: NUU (Other use, unclassified); USES (Uses)  
(solvent; preparation, characterization and pre-clin. evaluation of oral HIV-1 vaccine based on branched peptide immunogen entrapped in **controlled-release** microparticles)

IT 26780-50-7, Poly(DL-lactide-co-glycolide)

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(preparation, characterization and pre-clin. evaluation of oral HIV-1 vaccine based on branched peptide immunogen entrapped in **controlled-release** microparticles)

RN 26780-50-7 HCAPLUS

CN 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 1,4-dioxane-2,5-dione (9CI) (CA INDEX NAME)

CM 1

CRN 502-97-6

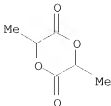
CMF C4 H4 O4



CM 2

CRN 95-96-5

CMF C6 H8 O4



IT 75-09-2, Dichloromethane, uses

RL: NUU (Other use, unclassified); USES (Uses)  
(solvent; preparation, characterization and pre-clin. evaluation of oral HIV-1 vaccine based on branched peptide immunogen entrapped in **controlled-release** microparticles)

RN 75-09-2 HCAPLUS

CN Methane, dichloro- (8CI, 9CI) (CA INDEX NAME)

CL-CH<sub>2</sub>-CL

L114 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1995:640933 HCAPLUS  
 DN 123:17955  
 ED Entered STN: 28 Jun 1995  
 TI Method for preparing microspheres comprising a fluidized bed drying step  
 IN Cleland, Jeffrey L.; Jones, Andrew J.; Powell, Michael Frank  
 PA Genentech, Inc., USA  
 SO PCT Int. Appl., 24 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K009-16  
 CC 63-6 (Pharmaceuticals)  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9511009	A1	19950427	WO 1994-US11678	19941013 <--
	W: AU, BR, CA, JP				
	RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2172508	AA	19950427	CA 1994-2172508	19941013 <--
	AU 9480174	A1	19950508	AU 1994-80174	19941013 <--
	EP 724433	A1	19960807	EP 1994-931369	19941013 <--
	EP 724433	B1	19981230		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 09504026	T2	19970422	JP 1994-512076	19941013 <--
	AT 175110	E	19990115	AT 1994-931369	19941013 <--
	US 6080429	A	20000627	US 1997-966850	19971107 <--
PRAI	US 1993-142257	A	19931022 <--		
	US 1993-143313	A	19931025 <--		
	WO 1994-US11678	W	19941013 <--		
	US 1996-650364	B1	19960520		
AB	A method for encapsulating an active agent in microspheres comprises (a) dissolving a polymer in an organic solvent, (b) adding active agent to produce an emulsion or suspension, (c) adding this mixture to an emulsification bath to produce microspheres, (d) hardening the microspheres, and (e) drying the microspheres in a fluidized bed. Thus, a buffered solution (154 mg/mL) of recombinant glycoprotein gp120 from HIV-1 strain MN was homogenized with a solution of DL-lactide/glycolide copolymer in CH <sub>2</sub> Cl <sub>2</sub> (0.3 or 0.6 g/mL), and 10 mL of this emulsion was homogenized with 900 mL 10% poly(vinyl alc.) solution containing 1.5% CH <sub>2</sub> Cl <sub>2</sub> to produce a water-in-oil-in-water emulsion, which was transferred to a hardening bath of filtered water for 1 h. The microspheres were concentrated, diafiltered, concentrated to dryness, and dried in a fluidized bed in a stream of N <sub>2</sub> . These microspheres showed a much smaller initial burst than microspheres prepared similarly but dried by lyophilization.				
ST	microsphere drug drying fluidized bed				
IT	Freeze drying				
	Solvents				
	(method for preparing microspheres with fluidized bed drying step)				
IT	Antigens				
	Proteins, biological studies				
	RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)				

- (method for preparing microspheres with fluidized bed drying step)
- IT Polyesters, biological studies  
Polymers, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(method for preparing microspheres with fluidized bed drying step)
- IT Immunostimulants  
(**adjuvants**, method for preparing microspheres with fluidized bed drying step)
- IT Drying  
(fluidized-bed, method for preparing microspheres with fluidized bed drying step)
- IT Sialoglycoproteins  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(gp120env, method for preparing microspheres with fluidized bed drying step)
- IT Virus, animal  
(human immunodeficiency 1, glycoprotein gp120 of; method for preparing microspheres with fluidized bed drying step)
- IT Pharmaceutical dosage forms  
(microspheres, method for preparing microspheres with fluidized bed drying step)
- IT Drying  
(vacuum, method for preparing microspheres with fluidized bed drying step)
- IT 9002-72-6, Growth hormone  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(human; method for preparing microspheres with fluidized bed drying step)
- IT 9002-89-5, Poly(vinyl alcohol) **26780-50-7, DL-Lactide/glycolide** copolymer 141256-04-4  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(method for preparing microspheres with fluidized bed drying step)
- IT 67-64-1, Acetone, uses **75-09-2, Methylene chloride**, uses 100-51-6, Benzyl alcohol, uses 141-78-6, Ethyl acetate, uses  
RL: NUU (Other use, unclassified); USES (Uses)  
(solvent; method for preparing microspheres with fluidized bed drying step)
- IT **26780-50-7, DL-Lactide/glycolide** copolymer  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(method for preparing microspheres with fluidized bed drying step)
- RN 26780-50-7 HCAPLUS
- CN 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 1,4-dioxane-2,5-dione (9CI) (CA INDEX NAME)

CM 1

CRN 502-97-6

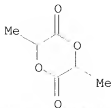
CMF C4 H4 O4



CM 2

CRN 95-96-5

CMF C6 H8 O4



IT 75-09-2, **Methylene chloride**, uses  
 RL: NUU (Other use, unclassified); USES (Uses)  
 (solvent; method for preparing microspheres with fluidized bed drying step)  
 RN 75-09-2 HCAPLUS  
 CN Methane, dichloro- (8CI, 9CI) (CA INDEX NAME)

C1-CH2-C1

L114 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1995:316163 HCAPLUS  
 DN 122:89472  
 ED Entered STN: 28 Jan 1995  
 TI Preparation of microparticles and method of immunization  
 IN O'Hagan, Derek Thomas; McGee, John Paul; Davis, Stanley Stewart  
 PA USA  
 SO PCT Int. Appl., 38 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM B01J013-02  
 ICS A61K009-14; A61K009-50; A61K039-385  
 CC 63-6 (Pharmaceuticals)  
 Section cross-reference(s): 15

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9427718	A1	19941208	WO 1994-US5834	19940524 <--
	W: AU, CA, FI, JP, NO, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9470441	A1	19941220	AU 1994-70441	19940524 <--
	US 5603960	A	19970218	US 1995-374751	19950602 <--
PRAI	GB 1993-10781		19930525 <--		
	WO 1994-US5834		19940524 <--		

AB The present invention describes a method for producing microparticles useful in the formulation of pharmaceutical compns. The present invention further describes a method of immunizing a mammal against diseases comprising administering to a mammal an effective amount of antigen containing microparticles. In particular, the present invention describes a method of potentiating an immune response in a mammal comprising administering an effective amount of a pharmaceutical composition to a mammal. The present invention further describes a **vaccine** comprising a pharmaceutical composition containing said microparticles. An antigen delivery system comprising microparticles containing entrapped antigens is further described by the present invention. A pharmaceutical composition comprising microparticles and a pharmaceutical carrier is also provided.

ST microparticle immunization; **vaccine** microparticle

IT **Vaccines**  
 (preparation of microparticles and method of immunization)

IT Antigens  
 Peptides, biological studies  
 Polyesters, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (preparation of microparticles and method of immunization)

IT Pharmaceutical dosage forms  
 (microparticles, preparation of microparticles and method of immunization)

IT 75-09-2, Dichloromethane, uses 141-78-6, Ethyl acetate, uses 142-82-5, Heptane, uses  
 RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); PROC (Process); USES (Uses)  
 (preparation of microparticles and method of immunization)

IT 26009-03-0, Polyglycolide 26023-30-3  
 26202-08-4, Polyglycolide 26680-10-4, Poly (DL-lactide) 26780-50-7, Glycolide-DL-lactide copolymer  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (preparation of microparticles and method of immunization)

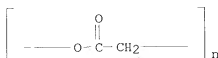
IT 75-09-2, Dichloromethane, uses  
 RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); PROC (Process); USES (Uses)  
 (preparation of microparticles and method of immunization)

RN 75-09-2 HCAPLUS  
 CN Methane, dichloro- (8CI, 9CI) (CA INDEX NAME)

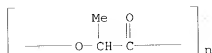
Cl-CH<sub>2</sub>-Cl

IT 26009-03-0, Polyglycolide 26023-30-3  
 26202-08-4, Polyglycolide 26780-50-7, Glycolide-DL-lactide copolymer  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (preparation of microparticles and method of immunization)

RN 26009-03-0 HCAPLUS  
 CN Poly[oxy(1-oxo-1,2-ethanediyl)] (9CI) (CA INDEX NAME)



RN 26023-30-3 HCAPLUS  
 CN Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] (8CI, 9CI) (CA INDEX NAME)



RN 26202-08-4 HCAPLUS  
 CN 1,4-Dioxane-2,5-dione, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 502-97-6  
 CMF C4 H4 O4



RN 26780-50-7 HCAPLUS  
 CN 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 1,4-dioxane-2,5-dione  
 (9CI) (CA INDEX NAME)

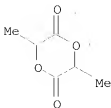
CM 1

CRN 502-97-6  
 CMF C4 H4 O4



CM 2

CRN 95-96-5  
 CMF C6 H8 O4



L114 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1994:442594 HCAPLUS

DN 121:42594

ED Entered STN: 23 Jul 1994

TI **Controlled release** of proteins from poly(L-lactic acid) coated poly(isobutyl cyanoacrylate) microcapsules

AU Park, Tae Gwan; Alonso, Maria J.; Langer, Robert

CS Dep. Chem. Eng., Massachusetts Inst. Technol., Cambridge, MA, 02139, USA

SO Journal of Applied Polymer Science (1994), 52(12), 1797-807

CODEN: JAPNAB; ISSN: 0021-8995

DT Journal

LA English

CC 63-5 (Pharmaceuticals)

AB Poly(L-lactic acid)-coated poly(iso-Bu cyanoacrylate)

(PIBCA) microcapsules containing protein mols. were prepared by a single-step procedure based on either a double-emulsion solvent evaporation method or a spray-drying method. First, an aqueous protein solution was emulsified in an organic phase of **methylene chloride** containing a wall-forming monomer (iso-Bu cyanoacrylate), various kinds of poly(L-lactic acid), and a surfactant. An immediate polymerization process of iso-Bu

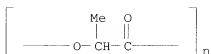


cyanoacrylate takes place at the W/O interface upon contact with hydroxide ion in the aqueous phase, leading to the formation of a PICBA wall around the aqueous droplets. This W/O emulsion was reemulsified in an aqueous solution to promote the solvent removal and, consequently, the precipitation of poly(L-lactic acid) onto PICBA microcapsules or was spray albumin, horseradish peroxidase, and tetanus toxoid, were encapsulated in these poly(L-lactic acid)-coated PICBA microcapsules, and then their release profiles were examined in vitro as a function of mol. weight of poly(L-lactic acid) and its copolymers with glycolic acid.

These formulations exhibited a low "burst" effect at initial incubation stages and released the proteins for extended periods of time.

S.c. injection of the tetanus toxoid-loaded microparticles into rats showed that the time course of immunization (antibody titer) can be controlled by the type of polymer matrixes used.

- ST controlled release protein microcapsule;  
poly(lactic acid) polyisobutyl cyanoacrylate microcapsule
- IT Solution rate  
(of proteins, from poly(lactic acid)-coated poly(iso-Bu cyanoacrylate) microcapsules)
- IT Proteins, biological studies  
RL: BIOL (Biological study)  
(poly(lactic acid)-coated poly(iso-Bu cyanoacrylate) microcapsules for controlled release of)
- IT Polyesters, biological studies  
RL: BIOL (Biological study)  
(lactic acid-based, poly(iso-Bu cyanoacrylate) microcapsules coated with, controlled release of proteins from)
- IT Pharmaceutical dosage forms  
(microcapsules, controlled release, poly(lactic acid)-coated poly(iso-Bu cyanoacrylate), for proteins)
- IT 26809-38-1, Poly(isobutyl cyanoacrylate)  
RL: BIOL (Biological study)  
(microcapsules, poly(lactic acid)-coated, controlled release of proteins from)
- IT 26023-30-3, Poly(DL-lactic acid)  
26100-51-6, Poly(DL-lactic acid)  
26161-42-2, Poly(L-lactic acid) 26811-96-1,  
Poly(L-lactic acid) 54512-07-1,  
Glycolic acid-L-lactic acid copolymer  
RL: BIOL (Biological study)  
(poly(iso-Bu cyanoacrylate) microcapsules coated with, controlled release of proteins from)
- IT 26023-30-3, Poly(DL-lactic acid)  
26100-51-6, Poly(DL-lactic acid)  
26161-42-2, Poly(L-lactic acid)  
54512-07-1, Glycolic acid-L-lactic acid copolymer  
RL: BIOL (Biological study)  
(poly(iso-Bu cyanoacrylate) microcapsules coated with, controlled release of proteins from)
- RN 26023-30-3 HCAPLUS  
CN Poly[oxy(1-methyl-2-oxo-1,2-ethanediy)] (8CI, 9CI) (CA INDEX NAME)



RN 26100-51-6 HCAPLUS

CN Propanoic acid, 2-hydroxy-, homopolymer (9CI) (CA INDEX NAME)

CM 1

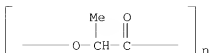
CRN 50-21-5

CMF C3 H6 O3



RN 26161-42-2 HCAPLUS

CN Poly[oxy[(1S)-1-methyl-2-oxo-1,2-ethanediyl]] (9CI) (CA INDEX NAME)



RN 54512-07-1 HCAPLUS

CN Propanoic acid, 2-hydroxy-, (2S)-, polymer with hydroxyacetic acid (9CI)  
(CA INDEX NAME)

CM 1

CRN 79-33-4

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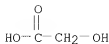
Absolute stereochemistry. Rotation (+).



CM 2

CRN 79-14-1

CMF C2 H4 O3



=&gt; d l115 all hitstr tot

L115 ANSWER 1 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:151479 HCAPLUS

DN 126:162266

ED Entered STN: 08 Mar 1997

TI Biocompatible and biodegradable nanoparticles designed for proteinaceous drug absorption and delivery

IN Grandfils, Christian; Jerome, Robert; Nihant, Nicole; Teyssie, Philippe

PA University of Liege, Belg.

SO Eur. Pat. Appl., 13 pp.

CODEN: EPXXDW

DT Patent

LA English

IC ICM A61K009-51

CC 63-6 (Pharmaceuticals)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 752245	A1	19970108	EP 1995-110445	19950705 <--
	EP 752245	B1	20020522		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	AT 217792	E	20020615	AT 1995-110445	19950705 <--
	PT 752245	T	20020930	PT 1995-95110445	19950705 <--
	ES 2177592	T3	20021216	ES 1995-110445	19950705 <--
	CA 2226166	AA	19970123	CA 1996-2226166	19960702 <--
	CA 2226166	C	20010508		
	WO 9702022	A1	19970123	WO 1996-EP2878	19960702 <--
	W: CA, JP, US				
	JP 11504655	T2	19990427	JP 1997-504807	19960702 <--
	JP 3486417	B2	20040113		
	US 5962566	A	19991005	US 1998-973863	19980507 <--
PRAI	EP 1995-110445	A	19950705	<--	
	WO 1996-EP2878	W	19960702		
AB	A polymer blend is obtained by intimate mixing a biocompatible polymer to form nanoparticles with a biocompatible interacting agent which is able to preserve the activity of the drug to be administered and to <b>control the release</b> of the drug to be administered. The polymer blend is an intermediate product for preparing nanoparticles which drugs can be adhered on or incorporated in. <b>Glycolide-DL-lactide</b> copolymer and Pluronic F68 were dissolved in <b>methylene chloride</b> and the solvent was let to evaporate under N. Cholesterol 3-sulfate was added to the polymer blend followed by DMSO for dissoln. Somatotropin was added to the solution and the suspension obtained was diluted with water and purified by ultrafiltration. The somatotropin immobilization efficiency in the concentrated latex suspension was 90 % and kinetics of in vitro <b>release</b> of the protein was studied.				
ST	polymer blend nanoparticle protein drug carrier; polyester Pluronic blend somatotropin nanoparticle				
IT	Polyesters, biological studies				
	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (biocompatible and biodegradable nanoparticles designed for proteinaceous drug absorption and delivery)				
IT	Proteins, specific or class				
	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (biol. active; biocompatible and biodegradable nanoparticles designed for proteinaceous drug absorption and delivery)				
IT	Drug delivery systems				
	(nanoparticles; biocompatible and biodegradable nanoparticles designed for proteinaceous drug absorption and delivery)				
IT	9002-72-6, Somatotropin <b>26023-30-3</b> , Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] <b>26680-10-4</b> , <b>Poly(lactide 26780-50-7</b> , <b>Glycolide-DL-lactide</b> copolymer <b>106392-12-5</b> , Pluronic				

F68 157170-88-2, 2-Hydroxyethyl methacrylate-DL-lactide graft copolymer

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(biocompatible and biodegradable nanoparticles designed for proteinaceous drug absorption and delivery)

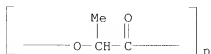
IT 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)]

26780-50-7, Glycolide-DL-lactide copolymer

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(biocompatible and biodegradable nanoparticles designed for proteinaceous drug absorption and delivery)

RN 26023-30-3 HCAPLUS

CN Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] (8CI, 9CI) (CA INDEX NAME)



RN 26780-50-7 HCAPLUS

CN 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 1,4-dioxane-2,5-dione (9CI) (CA INDEX NAME)

CM 1

CRN 502-97-6

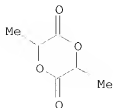
CMF C4 H4 O4



CM 2

CRN 95-96-5

CMF C6 H8 O4



L115 ANSWER 2 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1996:367770 HCAPLUS

DN 125:19065

ED Entered STN: 26 Jun 1996

TI Sustained-release preparation containing metal salt of a peptide

IN Igari, Yasutaka; Yamagata, Yutaka; Iinuma, Satoshi; Okada, Hiroaki

PA Takeda Chemical Industries, Ltd., Japan

SO PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DT Patent  
 LA English  
 IC ICM A61K009-16  
 ICS A61K009-50  
 CC 63-6 (Pharmaceuticals)  
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9607399	A1	19960314	WO 1995-JP1771	19950906 <--
	W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, US, UZ, VN				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2196184	AA	19960314	CA 1995-2196184	19950906 <--
	AU 9533990	A1	19960327	AU 1995-33990	19950906 <--
	AU 695323	B2	19980813		
	EP 779806	A1	19970625	EP 1995-930707	19950906 <--
	EP 779806	B1	20001108		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	CN 1157562	A	19970820	CN 1995-194963	19950906 <--
	BR 9509201	A	19971230	BR 1995-9201	19950906 <--
	EP 1002529	A1	20000524	EP 1999-203867	19950906 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
	AT 197398	E	20001111	AT 1995-930707	19950906 <--
	ES 2151079	T3	20001216	ES 1995-930707	19950906 <--
	PT 779806	T	20010228	PT 1995-95930707	19950906 <--
	RU 2181999	C2	20020510	RU 1997-105827	19950906 <--
	JP 08217691	A2	19960827	JP 1995-230841	19950908 <--
	FI 9700952	A	19970306	FI 1997-952	19970306 <--
	NO 9701030	A	19970306	NO 1997-1030	19970306 <--
	US 6376461	B1	20020423	US 1999-426716	19991026 <--
	US 2002058622	A1	20020516	US 2001-985925	20011106 <--
	US 2002168337	A1	20021114	US 2002-136328	20020502 <--
PRAI	JP 1994-216449	A	19940909 <--		
	JP 1994-310291	A	19941214 <--		
	JP 1993-153393	A	19930624 <--		
	US 1994-265124	B2	19940624 <--		
	EP 1995-930707	A3	19950906 <--		
	WO 1995-JP1771	W	19950906 <--		
	US 1996-644631	A1	19960422		
	US 1999-426716	A3	19991026		
	US 2001-985925	A1	20011106		
AB	A sustained-release preparation contain a water-insol. or slightly water-soluble				
	polyvalent metal salt of a water-soluble peptide type of physiol. active substance, except for an endothelin antagonist and a biodegradable polymer. To a solution of 3.6 g lactic acid-glycolic acid copolymer in 5 mL of				
	dichloromethane was added 420 mg of crude zinc salt of swine insulin (preparation given) in 5 mL of dichloromethane and stirred for 10 s, then this emulsion was poured in in 800 mL of 0.1% polyvinyl alc. and mixed at 6,000 rpm to yield an emulsion. The emulsion was stirred at room temperature for 3 h to volatilize the dichloromethane and the residue was dispersed in water and centrifuged to obtain microcapsules which were collected and re-dispersed in water in presence of 50 mg D-mannitol, then freeze-dried to give powder microcapsules. After s.c. injection of above microcapsules to rats, active swine insulin was detected in serum for 1 wk or more.				
ST	sustained release pharmaceutical metal salt peptide; insulin zinc sustained release microcapsule				

- IT Receptors  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(soluble; sustained-release preparation containing metal salt of a peptide)
- IT Animal growth regulators  
Antibodies  
Antigens  
Blood-coagulation factors  
Enzymes  
Hormones  
Interferons  
Lymphokines and Cytokines  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(sustained-release preparation containing metal salt of a peptide)
- IT Polymers, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(sustained-release preparation containing metal salt of a peptide)
- IT Polyesters, biological studies  
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(aliphatic, sustained-release preparation containing metal salt of a peptide)
- IT Hemopoietins  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(hematopoietic cell growth factors, sustained-release preparation containing metal salt of a peptide)
- IT Peptides, biological studies  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(metal salts, sustained-release preparation containing metal salt of a peptide)
- IT **Pharmaceutical dosage forms**  
(microcapsules, sustained-release, sustained-release preparation containing metal salt of a peptide)
- IT Transition metal compounds  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(salts, with peptides; sustained-release preparation containing metal salt of a peptide)
- IT **Pharmaceutical dosage forms**  
(sustained-release, sustained-release preparation containing metal salt of a peptide)
- IT Albumins, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(zinc complexes, sustained-release preparation containing metal salt of a peptide)
- IT Interferons  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
( $\alpha$ , sustained-release preparation containing metal salt of a peptide)
- IT 8049-62-5P, Zinc insulin 12629-01-5DP, Human growth hormone, zinc salt  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (sustained-release preparation containing metal salt of a peptide)

IT 9002-72-6, Growth hormone 9004-10-8, Insulin, biological studies  
 74381-53-6, Leuprolide acetate  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (sustained-release preparation containing metal salt of a peptide)

IT 557-34-6, Zinc acetate 759-73-9 1117-96-0, Diazoethane 1310-58-3,  
 Potassium hydroxide, reactions 7646-85-7, Zinc chloride, reactions  
 12629-01-5, Human growth hormone  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (sustained-release preparation containing metal salt of a peptide)

IT 50-21-5D, Lactic acid, Et esters, polymers  
 with glycolic acid 69-65-8, D-Mannitol  
 79-14-1D, polymers with Et lactate 26100-51-6,  
 Lactic acid homopolymer 34346-01-5,  
 Lactic acid-glycolic acid copolymer  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (sustained-release preparation containing metal salt of a peptide)

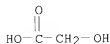
IT 143011-72-7P, Granulocyte colony stimulating factor  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (zinc salt; sustained-release preparation containing metal salt of a peptide)

IT 50-21-5D, Lactic acid, Et esters, polymers  
 with glycolic acid 79-14-1D, polymers with  
 Et lactate 26100-51-6, Lactic acid  
 homopolymer 34346-01-5, Lactic acid-glycolic acid copolymer  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (sustained-release preparation containing metal salt of a peptide)

RN 50-21-5 HCAPLUS  
 CN Propanoic acid, 2-hydroxy- (9CI) (CA INDEX NAME)



RN 79-14-1 HCAPLUS  
 CN Acetic acid, hydroxy- (9CI) (CA INDEX NAME)



RN 26100-51-6 HCAPLUS  
 CN Propanoic acid, 2-hydroxy-, homopolymer (9CI) (CA INDEX NAME)

CM 1

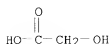
CRN 50-21-5  
 CMF C3 H6 O3



RN 34346-01-5 HCAPLUS  
 CN Propanoic acid, 2-hydroxy-, polymer with hydroxyacetic acid (9CI) (CA  
 INDEX NAME)

CM 1

CRN 79-14-1  
 CMF C2 H4 O3



CM 2

CRN 50-21-5  
 CMF C3 H6 O3



L115 ANSWER 3 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1996:252396 HCAPLUS  
 DN 124:270588  
 ED Entered STN: 30 Apr 1996  
 TI Slow-release pharmaceutical compositions containing 2-(8-dimethylaminooctylthio)-3-(2-thenoyl)-6-isopropylpyridine for Alzheimer's disease  
 IN Iwamoto, Nobuko; Tsunekawa, Yukiko; Mizuta, Hiroaki; Nakajima, Tooru  
 PA Yoshitomi Pharmaceutical Industries, Ltd., Japan  
 SO Jpn. Kokai Tokkyo Koho, 7 pp.  
 CODEN: JKXXAF  
 DT Patent  
 LA Japanese  
 IC ICM A61K031-44  
 ICS A61K009-16; A61K047-34; C07D409-06  
 CC 63-6 (Pharmaceuticals)  
 Section cross-reference(s): 1

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 08034732	A2	19960206	JP 1995-118144	19950517 <--
PRAI	JP 1994-102526		19940517 <--		
AB	Slow-release pharmaceutical compns. for Alzheimer's disease contain 2-(8-dimethylaminooctylthio)-3-(2-thenoyl)-6-isopropylpyridine or its acid addition salts as active ingredient and biocompatible polymers having average particle size 15-400 $\mu\text{m}$ . Thus, 2-(8-dimethylaminooctylthio)-3-(2-thenoyl)-6-isopropylpyridine citrate 33.7 and dl-poly(lactic acid (mol. weight 20,000) 189.2 mg were dissolved in 1 mL dichloromethane and homogenized with 0.1 M Na acetate-containing 0.5%				



- polyvinyl alc.(250 mL) to form oil/water-type emulsion. After s.c. or i.m. administration to rats, blood concentration of the active ingredient remained high for up to 1 mo.
- ST slow release pharmaceutical thenoylisopropylpyridine Alzheimer disease; thenoylisopropylpyridine deriv Alzheimer disease
- IT Drug bioavailability  
Particle size  
Solution rate  
(slow-release pharmaceutical compns. containing 2-(8-dimethylaminooctylthio)-3-(2-thenoyl)-6-isopropylpyridine and biocompatible polymers for Alzheimer's disease)
- IT Polymers, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(slow-release pharmaceutical compns. containing 2-(8-dimethylaminooctylthio)-3-(2-thenoyl)-6-isopropylpyridine and biocompatible polymers for Alzheimer's disease)
- IT Mental disorder  
(Alzheimer's disease, slow-release pharmaceutical compns. containing 2-(8-dimethylaminooctylthio)-3-(2-thenoyl)-6-isopropylpyridine and biocompatible polymers for Alzheimer's disease)
- IT **Pharmaceutical dosage forms**  
(injections, i.m. or s.c.; **slow-release** pharmaceutical compns. containing 2-(8-dimethylaminooctylthio)-3-(2-thenoyl)-6-isopropylpyridine and biocompatible polymers for Alzheimer's disease)
- IT **26100-51-6, dl-Polylactic acid**  
**26124-68-5, Polyglycolic acid** 129184-48-1,  
2-(8-Dimethylaminooctylthio)-3-(2-thenoyl)-6-isopropylpyridine  
143984-17-2, 2-(8-Dimethylaminooctylthio)-3-(2-thenoyl)-6-isopropylpyridine p-toluenesulfonate 143984-30-9, 2-(8-Dimethylaminooctylthio)-3-(2-thenoyl)-6-isopropylpyridine citrate  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(slow-release pharmaceutical compns. containing 2-(8-dimethylaminooctylthio)-3-(2-thenoyl)-6-isopropylpyridine and biocompatible polymers for Alzheimer's disease)
- IT **26100-51-6, dl-Polylactic acid**  
**26124-68-5, Polyglycolic acid**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(slow-release pharmaceutical compns. containing 2-(8-dimethylaminooctylthio)-3-(2-thenoyl)-6-isopropylpyridine and biocompatible polymers for Alzheimer's disease)
- RN 26100-51-6 HCAPLUS
- CN Propanoic acid, 2-hydroxy-, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 50-21-5

CMF C3 H6 O3

OH

Me-CH-CO<sub>2</sub>H

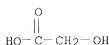
RN 26124-68-5 HCAPLUS

CN Acetic acid, hydroxy-, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 79-14-1

CMF C2 H4 O3



L115 ANSWER 4 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1996:44091 HCAPLUS

DN 124:97546

ED Entered STN: 23 Jan 1996

TI Somatostatin containing biodegradable microspheres prepared by a modified solvent evaporation method based on W/O/W-multiple emulsions

AU Herrmann, Joachim; Bodmeier, Roland

CS College of Pharmacy, The University of Texas at Austin, Austin, TX, 78712, USA

SO International Journal of Pharmaceutics (1995), 126(1,2), 129-38

CODEN: IJPHDE; ISSN: 0378-5173

PB Elsevier

DT Journal

LA English

CC 63-6 (Pharmaceuticals)

AB Biodegradable polyester microspheres containing somatostatin acetate, a peptide drug, were prepared by a modified solvent evaporation method based on the

formation of multiple W/O-W-emulsions. The resulting microspheres were characterized with respect to drug loading, **encapsulation** efficiency and morphol. characteristics. Various methods for extracting the peptide from the microspheres were compared. Of all parameters investigated, factors affecting the properties of the primary W/O-emulsion, such as the phase volume ratio and total volume, were of major importance. A small volume of internal aqueous phase and an intermediate volume

of organic solvent were favorable to achieve high drug **encapsulation** efficiencies. Replacing **methylene chloride** as an organic solvent with Et acetate reduced the **encapsulation** efficiency and resulted in more porous microspheres. Except for microspheres prepared with very low mol. weight polymers, the **encapsulation** efficiency was not affected by the polymer type (**poly(L-lactide)**, **poly(DL-lactide)**, **poly(DL-lactide/glycolide)**) and mol. weight. The preparation conditions substantially affected the morphol. and porosity of the microspheres.

ST peptide **encapsulation** biodegradable polymer microsphere; somatostatin **encapsulation** biodegradable polyester microsphere

IT Polymers, biological studies

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(biodegradable; **microencapsulation** of peptide drugs in biodegradable polymer microspheres prepared by modified solvent evaporation method based on W/O/W-multiple emulsions)

IT Solvents

(evaporation; **microencapsulation** of somatostatin in biodegradable polyester microspheres prepared by modified solvent evaporation method based on W/O/W-multiple emulsions)

IT Peptides, biological studies

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(**microencapsulation** of peptide drugs in biodegradable polymer microspheres prepared by modified solvent evaporation method based on W/O/W-multiple emulsions)

IT Porosity

(**microencapsulation** of somatostatin in biodegradable polyester microspheres prepared by modified solvent evaporation method based

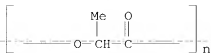
- on W/O/W-multiple emulsions)
- IT Polyesters, biological studies  
 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (microencapsulation of somatostatin in biodegradable polyester microspheres prepared by modified solvent evaporation method based on W/O/W-multiple emulsions)
- IT Polyesters, biological studies  
 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (hydroxycarboxylic acid-based, microencapsulation of somatostatin in biodegradable polyester microspheres prepared by modified solvent evaporation method based on W/O/W-multiple emulsions)
- IT Polyesters, biological studies  
 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (lactic acid-based, microencapsulation of somatostatin in biodegradable polyester microspheres prepared by modified solvent evaporation method based on W/O/W-multiple emulsions)
- IT Encapsulation  
 (micro-, microencapsulation of somatostatin in biodegradable polyester microspheres prepared by modified solvent evaporation method based on W/O/W-multiple emulsions)
- IT Pharmaceutical dosage forms  
 (microspheres, controlled-release, microencapsulation of somatostatin in biodegradable polyester microspheres prepared by modified solvent evaporation method based on W/O/W-multiple emulsions)
- IT 67-56-1, Methanol, uses 75-05-8, Acetonitrile, uses 75-09-2, Methylene chloride, uses 141-78-6, Ethyl acetate, uses  
 RL: NUU (Other use, unclassified); USES (Uses)  
 (microencapsulation of somatostatin in biodegradable polyester microspheres prepared by modified solvent evaporation method based on W/O/W-multiple emulsions)
- IT 26023-30-3 26161-42-2 26680-10-4, Poly(DL-lactide) 26780-50-7, DL-Lactide-glycolide copolymer 33135-50-1, Poly(L-lactide)  
 ) 51110-01-1, Somatostatin  
 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (microencapsulation of somatostatin in biodegradable polyester microspheres prepared by modified solvent evaporation method based on W/O/W-multiple emulsions)
- IT 9002-89-5, Polyvinyl alcohol  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (microencapsulation of somatostatin in biodegradable polyester microspheres prepared by modified solvent evaporation method based on W/O/W-multiple emulsions)
- IT 75-09-2, Methylene chloride, uses  
 RL: NUU (Other use, unclassified); USES (Uses)  
 (microencapsulation of somatostatin in biodegradable polyester microspheres prepared by modified solvent evaporation method based on W/O/W-multiple emulsions)
- RN 75-09-2 HCAPLUS  
 CN Methane, dichloro- (8CI, 9CI) (CA INDEX NAME)

Cl-CH<sub>2</sub>-Cl

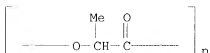
- IT 26023-30-3 26161-42-2 26780-50-7, DL-Lactide-glycolide copolymer  
 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic

use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (microencapsulation of somatostatin in biodegradable  
 polyester microspheres prepared by modified solvent evaporation method based  
 on W/O/W-multiple emulsions)

RN 26023-30-3 HCAPLUS  
 CN Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] (8CI, 9CI) (CA INDEX NAME)



RN 26161-42-2 HCAPLUS  
 CN Poly[oxy(1S)-1-methyl-2-oxo-1,2-ethanediyl]] (9CI) (CA INDEX NAME)



RN 26780-50-7 HCAPLUS  
 CN 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 1,4-dioxane-2,5-dione  
 (9CI) (CA INDEX NAME)

CM 1

CRN 502-97-6

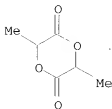
CMF C4 H4 O4



CM 2

CRN 95-96-5

CMF C6 H8 O4



L115 ANSWER 5 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1996:38799 HCAPLUS

DN 124:66652

ED Entered STN: 20 Jan 1996

TI Modulated-release pharmaceuticals containing a biocompatible polymer

matrix and a metal cation  
 IN Bernstein, Howard; Zhang, Yan; Khan, M. Amin; Tracy, Mark A.  
 PA Alkermes Controlled Therapeutics, Inc., USA  
 SO PCT Int. Appl., 70 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K009-16  
 ICS A61K009-70  
 CC 63-6 (Pharmaceuticals)  
 FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9529664	A1	19951109	WO 1995-US5511	19950503 <--
	W:	AM, AT, AU, BE, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT			
	RW:	KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	US 5656297	A	19970812	US 1994-237057	19940503 <--
	AU 9524674	A1	19951129	AU 1995-24674	19950503 <--
	AU 688506	B2	19980312		
	EP 758227	A1	19970219	EP 1995-918942	19950503 <--
	EP 758227	B1	20040114		
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE			
	JP 10504017	T2	19980414	JP 1995-528506	19950503 <--
	US 5912015	A	19990615	US 1998-56566	19980407 <--
	US 6368630	B1	20020409	US 1999-274613	19990323 <--
	US 2002168410	A1	20021114	US 2002-39285	20020103 <--
PRAI	US 1994-237057	A2	19940503	<--	
	US 1992-849754	B2	19920312	<--	
	WO 1995-US5511	W	19950503	<--	
	US 1996-727531	A1	19961022		
	US 1998-56566	A1	19980407		
	US 1999-274613	A1	19990323		
AB	A composition for the modulated release of a biol. active agent comprises a biocompatible polymeric matrix, a biol. active agent which is dispersed within the polymeric matrix, and a metal cation component which is dispersed within the polymeric matrix, whereby the metal cation component modulates the release of the biol. active agent from the polymeric matrix. A 10 mM solution of zinc acetate dihydrate was added to interferon- $\alpha$ 2, b (I) to obtain a final concentration of 1.3 mg/mL I, then the pH was adjusted				
to	7.1 with acetic acid. The above stabilized Zn-I suspension was micronized, frozen, and lyophilized to obtain I powder. Zinc carbonate and I powder were added in different proportions to a solution of 0.4g poly(lactide-glycolide) (II) in 4mL methylene chloride and then were microencapsulated in II to form I microspheres. Microsphere doses of 0.9 mg/kg were injected into the intrascapular region of the rats and blood concentration of I was measured at different times. The sustained-release level of immunol. active I was modulated depending upon the ratio of zinc carbonate to Zn-I in the microspheres, the higher the ratio of zinc carbonate demonstrated lower release rates of I from the microspheres.				
ST	pharmaceutical modulated release polymer metal cation; zinc carbonate interferon sustained release microsphere				
IT	Acrylic polymers, biological studies				
	Animal growth regulators				
	Cations				
	Interferons				

Polyanhydrides

Proteins, biological studies

Urethane polymers, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(modulated-release pharmaceuticals containing biocompatible polymer matrix and metal cation)

IT **Pharmaceutical dosage forms**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(films, sustained-release,

modulated-release pharmaceuticals containing biocompatible polymer matrix and metal cation)

IT **Lymphokines and Cytokines**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(interleukins, modulated-release pharmaceuticals containing biocompatible polymer matrix and metal cation)

IT **Pharmaceutical dosage forms**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(microspheres, sustained-release,

modulated-release pharmaceuticals containing biocompatible polymer matrix and metal cation)

IT **Polyethers, biological studies**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(ortho ester group-containing, modulated-release pharmaceuticals containing biocompatible polymer matrix and metal cation).

IT **Pharmaceutical dosage forms**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pellets, sustained-release,

modulated-release pharmaceuticals containing biocompatible polymer matrix and metal cation)

IT **Polyesters, biological studies**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(polyamide-, modulated-release pharmaceuticals containing biocompatible polymer matrix and metal cation)

IT **Polyamides, biological studies**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(polyester-, modulated-release pharmaceuticals containing biocompatible polymer matrix and metal cation)

IT **Polyesters, biological studies**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(polyether-, modulated-release pharmaceuticals containing biocompatible polymer matrix and metal cation)

IT **Alkenes, biological studies**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(polymers, chlorosulfonate; modulated-release pharmaceuticals containing biocompatible polymer matrix and metal cation)

IT **Lymphokines and Cytokines**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(tumor necrosis factor, modulated-release pharmaceuticals containing biocompatible polymer matrix and metal cation)

IT **Interferons**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

( $\alpha$ , 2, b; modulated-release pharmaceuticals containing biocompatible polymer matrix and metal cation)

IT 9001-99-4

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(A; modulated-release pharmaceuticals containing biocompatible polymer matrix and metal cation)

IT 74-85-1D, Ethene, polymers with vinyl acetate and acyl-substituted

cellulose acetate 108-05-4D, Acetic acid ethenyl ester, polymers with

ethylene and acyl-substituted cellulose acetate 142-72-3, Magnesium

acetate 471-34-1, Calcium carbonate, biological studies 546-46-3, Zinc

citrate 546-93-0, Magnesium carbonate 557-34-6, Zinc acetate

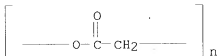
1309-42-8, Magnesium hydroxide 3486-35-9, Zinc carbonate 5970-45-6, Zinc acetate dihydrate 7487-88-9, Magnesium sulfate, biological studies 7646-85-7, Zinc chloride, biological studies 7733-02-0, Zinc sulfate 7779-25-1, Magnesium citrate 7786-30-3, Magnesium chloride, biological studies 9002-60-2, Acth, biological studies 9002-86-2, Pvc 9003-53-6 9004-35-7D, acyl-substituted polymers with ethylene and vinyl acetate 9026-81-7, Nuclease 11096-26-7, Erythropoietin 12629-01-5, Human growth hormone 24980-41-4, Polycaprolactone 24981-14-4, Polyvinyl fluoride 25232-42-2, Poly(vinyl imidazole) 25248-42-4, Polycaprolactone 25322-68-3 **26009-03-0, Polyglycolide** **26023-30-3**, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] **26100-51-6, Poly(lactic acid)** **26124-68-5, Poly(glycolic acid)** **26202-08-4, Polyglycolide** 26680-10-4, **Poly(lactide)** 26780-50-7, **Poly(glycolide-lactide)** 62683-29-8, Colony-stimulating factor  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (modulated-release pharmaceuticals containing biocompatible polymer matrix and metal cation)

IT **26009-03-0, Polyglycolide 26023-30-3**, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] **26100-51-6**, **Poly(lactic acid) 26124-68-5**, **Poly(glycolic acid) 26202-08-4**, **Polyglycolide 26780-50-7, Poly(glycolide-lactide)**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (modulated-release pharmaceuticals containing biocompatible polymer matrix and metal cation)

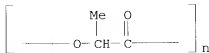
RN 26009-03-0 HCAPLUS

CN Poly[oxy(1-oxo-1,2-ethanediyl)] (9CI) (CA INDEX NAME)



RN 26023-30-3 HCAPLUS

CN Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] (8CI, 9CI) (CA INDEX NAME)



RN 26100-51-6 HCAPLUS

CN Propanoic acid, 2-hydroxy-, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 50-21-5

CMF C3 H6 O3



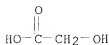
RN 26124-68-5 HCAPLUS

CN Acetic acid, hydroxy-, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 79-14-1

CMF C2 H4 O3



RN 26202-08-4 HCAPLUS

CN 1,4-Dioxane-2,5-dione, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 502-97-6

CMF C4 H4 O4



RN 26780-50-7 HCAPLUS

CN 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 1,4-dioxane-2,5-dione (9CI) (CA INDEX NAME)

CM 1

CRN 502-97-6

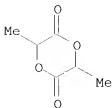
CMF C4 H4 O4



CM 2

CRN 95-96-5

CMF C6 H8 O4





AN 1995:1003552 HCAPLUS  
 DN 124:66431  
 ED Entered STN: 26 Dec 1995  
 TI Prediction of solvent removal profile and effect on properties for  
 peptide-loaded PLGA microspheres prepared by solvent  
 extraction/evaporation method  
 AU Li, Wen-I; Anderson, Kimberly W.; Mehta, Rahul C.; DeLuca, Patrick P.  
 CS Department of Chemical Engineering, Pennsylvania State University,  
 University Park, PA, 16802, USA  
 SO Journal of Controlled Release (1995); 37(3), 199-214  
 CODEN: JCREEC; ISSN: 0168-3659  
 PB Elsevier  
 DT Journal  
 LA English  
 CC 63-5 (Pharmaceuticals)  
 AB Using a predictive math. model, several important extrinsic process  
 variables were varied to simulate the process dynamics of microsphere  
 formation. These included the composition profile in the dispersed phase, the  
 solvent concentration profile in the continuous phase and the solvent removal  
 profile in the dispersed phase. By superimposing the composition profile in  
 the dispersed phase with the phase transition boundary, the progression of  
 phase transition in microsphere formation can be evaluated. Low dispersed  
 phase/continuous phase ratio, high continuous phase-addition rate, high  
 temperature, high heating rate and high initial polymer concentration in the  
 dispersed  
 phase contributed to enhanced solvent removal. The higher solvent removal  
 led to a heterogeneous composition distribution in the dispersed phase and the  
 early cross-over of the gelation point (viscous boundary) of the periphery  
 region which initiates the onset of solidification in this region. These  
 phenomena resulted in an increasing pore size, lower surface area, denser  
 periphery, higher residual solvent and slower drug release. In addition, the  
 progress toward the glassy boundary may also play a major role in the  
 ultimate solvent residual. Slow solvent removal gave rise to a  
 homogeneous distribution of the components in the dispersed phase due to  
 the delay of hardening. The extrinsic manageable parameters could be  
 varied during microsphere formation to obtain the desired rate of solvent  
 removal as well as the desired microsphere properties. The math. model  
 was used to simulate such conditions to facilitate the exptl. design for  
 the desired microsphere properties.  
 ST peptide polyester microsphere solvent removal modeling; **glycolide**  
**lactide** copolymer **microencapsulation** solvent removal;  
**controlled release** peptide polyester microsphere  
 IT Evaporation  
 Extraction  
 Pore  
 Simulation and Modeling, physicochemical  
 Solvents  
 Surface area  
 (modeling of solvent removal profile and effect on properties for  
 peptide-loaded PLGA microspheres prepared by solvent extraction/evaporation  
 method)  
 IT Peptides, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (modeling of solvent removal profile and effect on properties for  
 peptide-loaded PLGA microspheres prepared by solvent extraction/evaporation  
 method)  
 IT Polyesters, biological studies  
 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic  
 use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (hydroxycarboxylic acid-based, modeling of solvent removal profile and  
 effect on properties for peptide-loaded PLGA microspheres prepared by  
 solvent extraction/evaporation method)  
 IT **Encapsulation**

(micro-, modeling of solvent removal profile and effect on properties for peptide-loaded PLGA microspheres prepared by solvent extraction/evaporation method)

IT **Pharmaceutical dosage forms**

(**microspheres, controlled-release**, modeling of solvent removal profile and effect on properties for peptide-loaded PLGA microspheres prepared by solvent extraction/evaporation method)

IT 67-56-1, Methanol, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (cosolvent; modeling of solvent removal profile and effect on properties for peptide-loaded PLGA microspheres prepared by solvent extraction/evaporation method)

IT **26780-50-7, Poly(glycolide-co-lactide**

)  
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (modeling of solvent removal profile and effect on properties for peptide-loaded PLGA microspheres prepared by solvent extraction/evaporation method)

IT **75-09-2, Methylene chloride**, biological studies

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (solvent; modeling of solvent removal profile and effect on properties for peptide-loaded PLGA microspheres prepared by solvent extraction/evaporation method)

method)

IT **26780-50-7, Poly(glycolide-co-lactide**

)  
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (modeling of solvent removal profile and effect on properties for peptide-loaded PLGA microspheres prepared by solvent extraction/evaporation method)

method)

RN 26780-50-7 HCAPLUS

CN 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 1,4-dioxane-2,5-dione (9CI) (CA INDEX NAME)

CM 1

CRN 502-97-6

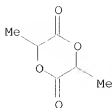
CMF C4 H4 O4



CM 2

CRN 95-96-5

CMF C6 H8 O4



IT 75-09-2, Methylene chloride, biological studies  
 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (solvent; modeling of solvent removal profile and effect on properties for peptide-loaded PLGA microspheres prepared by solvent extraction/evaporation method)  
 RN 75-09-2 HCAPLUS  
 CN Methane, dichloro- (8CI, 9CI) (CA INDEX NAME)

Cl- CH<sub>2</sub>-Cl

L115 ANSWER 7 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:997353 HCAPLUS

DN 124:37717

ED Entered STN: 22 Dec 1995

TI **Controlled-release** biodegradable microspheres and method of preparation

IN Arola, Rosa; Asin, Miguel Angel; Ferret, Eulalia; Goutay, Eric; Perez, Amadeo; Tarin, Pere

PA Pierre Fabre Medicament, Fr.

SO PCT Int. Appl., 24 pp.

CODEN: PIXXD2

DT Patent

LA French

IC ICM A61K009-50

ICS A61K009-16

CC 63-6 (Pharmaceuticals)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9528149	A1	19951026	WO 1995-FR485	19950413 <--
	W: AU, CA, JP, NZ, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	FR 2718642	A1	19951020	FR 1994-4511	19940415 <--
	FR 2718642	B1	19960712		
	CA 2187898	AA	19951026	CA 1995-2187898	19950413 <--
	AU 9523478	A1	19951110	AU 1995-23478	19950413 <--
	AU 698796	B2	19981105		
	EP 804173	A1	19971105	EP 1995-917394	19950413 <--
	EP 804173	B1	19981028		
	R: AT, BE, CH, DE, DK, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	JP 09512002	T2	19971202	JP 1995-526769	19950413 <--
	AT 172639	E	19981115	AT 1995-917394	19950413 <--
PRAI	FR 1994-4511		19940415	<--	
	WO 1995-FR485		19950413	<--	

AB A method for the preparation of a pharmaceutical composition in the form of **controlled-release** microspheres, **releasing** at

least one water soluble active ingredient is disclosed. The method comprises the steps of dissolving the active ingredient in a suitable quantity of water; emulsifying the aqueous solution containing the active ingredient with a solution of at least a D,L-lactide-co-glycolide-type matrix copolymer (I) in a chlorinated hydrocarbon further containing a low mol. weight **polylactide release-modulating agent**, which results in a first microfine and homogeneous emulsion; emulsifying the first emulsion thus obtained in an external aqueous phase, containing a surface active agent; and removing and evaporating the solvent to produce microspheres which are recovered after filtering, washing and drying. Thus, 20 mg tartrazine (II) was dissolved in 1mL water and the solution was mixed with 10mL of CH<sub>2</sub>Cl<sub>2</sub> containing 20% I and 40% **poly(DL-lactide)** to obtain an emulsion. This emulsion was emulsified with 1L solution containing 4% PVP and 0.25% ethoxylated sorbitan monooleate followed by evaporation of the solvents to obtain microspheres which was separated and dried. The amount of II released from the microspheres after 48 h at pH = 7.4 and 37° was 102.3%.

ST **controlled release biodegradable pharmaceutical microsphere polylactide; tartrazine controlled release pharmaceutical microsphere polylactide**

IT Surfactants  
(**controlled-release biodegradable microspheres comprising polylactides**)

IT Hydrocarbons, uses  
RL: NUU (Other use, unclassified); USES (Uses)  
(chloro, **controlled-release biodegradable microspheres comprising polylactides**)

IT **Pharmaceutical dosage forms**  
(**microspheres, controlled-release, controlled-release biodegradable microspheres comprising polylactides**)

IT 50-56-6, Oxytocin, biological studies 54-21-7, Sodium salicylate 57-22-7, Vincristine 59-05-2, Methotrexate 60-54-8, Tetracycline 69-53-4, Ampicillin 75-09-2, **Methylene chloride**, biological studies 154-93-8, Carmustin 1393-25-5, Secretin 1403-66-3, Gentamycin 1934-21-0, Tartrazine 3778-73-2, Ifosfamide 9002-62-4, Prolactin, biological studies 9002-67-9, Luteinizing hormone 9002-72-6, Growth hormone 9003-39-8, Pvp 9005-65-6, Ethoxylated sorbitan monooleate 9007-12-9, Calcitonin 11000-17-2, Vasopressin 15307-79-6, Sodium diclofenac 15663-27-1, Cisplatin 18559-94-9, Salbutamol 20830-81-3, Daunorubicin 23214-92-8, Doxorubicin 26023-30-3 26159-34-2, Sodium naproxen 26680-10-4, **Poly(DL-lactide)** 26780-50-7, D,L-Lactide-glycolide copolymer 26787-78-0, Amoxicillin 32986-56-4, Tobramycin 37517-28-5, Amikacin 51022-70-9, Salbutamol sulfate 51110-01-1, Somatostatin 53643-48-4, Vindesine 56420-45-2, Epirubicin 71486-22-1, Vinorelbine

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(**controlled-release biodegradable microspheres comprising polylactides**)

IT 75-09-2, **Methylene chloride**, biological studies 26023-30-3 26780-50-7, D,L-Lactide-glycolide copolymer

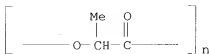
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(**controlled-release biodegradable microspheres comprising polylactides**)

RN 75-09-2 HCAPLUS

CN Methane, dichloro- (8CI, 9CI) (CA INDEX NAME)

Cl-CH<sub>2</sub>-Cl.

RN 26023-30-3 HCAPLUS  
 CN Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] (8CI, 9CI) (CA INDEX NAME)



RN 26780-50-7 HCAPLUS  
 CN 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 1,4-dioxane-2,5-dione (9CI) (CA INDEX NAME)

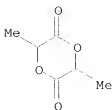
CM 1

CRN 502-97-6  
 CMF C4 H4 O4



CM 2

CRN 95-96-5  
 CMF C6 H8 O4



L115 ANSWER 8 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1995:721419 HCAPLUS  
 DN 123:93332  
 ED Entered STN: 05 Aug 1995  
 TI Rod-like **controlled-release** drug implants  
 IN Fujioka, Keiji; Hirasawa, Kenji; Kajiware, Masako; Sano, Akihiro;  
 Sugawara, Syuichi; Urabe, Yosuke  
 PA Dow Corning Asia, Ltd., Japan; Sumitomo Pharmaceuticals Co., Ltd.  
 SO Eur. Pat. Appl., 18 pp.  
 CODEN: EPXXDW  
 DT Patent  
 LA English  
 IC ICM A61K009-20  
 CC 63-6 (Pharmaceuticals)  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 659406	A2	19950628	EP 1994-120709	19941227 <--
	EP 659406	A3	19951115		
	EP 659406	B1	20000322		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 07187994	A2	19950725	JP 1993-331467	19931227 <--
	CA 2139058	AA	19950628	CA 1994-2139058	19941223 <--
	WO 9517881	A1	19950706	WO 1994-JP2208	19941226 <--
	W: AM, AU, BB, BG, BR, BY, CN, CZ, EE, FI, GE, HU, KE, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, UZ, VN				
	RW: KE, MW, SD, SZ, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9512809	A1	19950717	AU 1995-12809	19941226 <--
	AU 686713	B2	19980212		
	CN 1142763	A	19970212	CN 1994-195010	19941226 <--
	CN 1107497	B	20030507		
	AT 190836	E	20000415	AT 1994-120709	19941227 <--
	PT 659406	T	20000630	PT 1994-94120709	19941227 <--
	ES 2146633	T3	20000816	ES 1994-120709	19941227 <--
	US 5851547	A	19981222	US 1996-762847	19961210 <--
PRA1	JP 1993-331467	A	19931227 <--		
	US 1994-362623	B1	19941222 <--		
	WO 1994-JP2208	W	19941226 <--		

AB A rod-like drug formulation for producing sustained therapeutic efficacy comprises (a) a nondisintegrating inner layer comprised of a biocompatible material that contains uniformly dispersed water-soluble drug and (b) an outer layer comprised of a biocompatible material that surrounds the circumference of the inner layer, is impermeable to water, and is capable of controlling the swelling of the inner layer. The ratio of the axial length of the drug formulation to the cross-sectional diameter of the inner layer is one or more and one or both ends of the inner layer are open so as to come into direct contact with the external environment. For example, tetracycline-HCl was dispersed in **methylene chloride** solution of ethylene-vinyl acetate copolymer and cooled to solidification. The material was dried and cut into narrow strips, which were immersed in a **methylene chloride** solution of **glycolic acid-lactic acid** copolymer. After drying them, both ends were cut off to yield a drug formulation having an inner layer size of 5 mm x 0.9 mm x 10 mm and an outer layer thickness of 0.14 mm.

ST **controlled release** drug implant rod polymer

IT  
 Albumins, biological studies  
 Alkylating agents, biological  
 Amino acids, biological studies  
 Animal growth regulators  
 Antibodies  
 Blood-coagulation factors  
 Enzymes  
 Glycoproteins, biological studies  
 Hormones  
 Immunosuppressants  
 Inflammation inhibitors  
 Interferons  
 Lymphokines and Cytokines  
 Neoplasm inhibitors  
 Nucleic acids  
 Peptides, biological studies  
 Polyanhydrides  
 Polyesters, biological studies  
 Polysaccharides, biological studies  
 Proteins, biological studies

Rubber, silicone, biological studies  
 Salts, biological studies  
 Siloxanes and Silicones, biological studies  
 Urethane polymers, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (rod-like **controlled-release** drug implants)

IT Proteins, specific or class  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (CAM, rod-like **controlled-release** drug implants)

IT Hemopoietins  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (hematopoietic cell growth factors, rod-like **controlled-release** drug implants)

IT **Pharmaceutical dosage forms**  
 (implants, rod-like **controlled-release** drug implants)

IT 64-75-5, Tetracycline hydrochloride 79-10-7D, 2-Propenoic acid, derivs., polymers 79-41-4D, derivs., polymers 9002-84-0, Polytetrafluoroethylene 9002-88-4, Polyethylene 9002-89-5, Polyvinyl alcohol 9003-07-0, Polypropylene 24937-78-8, Ethylene-vinyl acetate copolymer **34346-01-5, Lactic acid-glycolic acid** copolymer  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (rod-like **controlled-release** drug implants)

IT **34346-01-5, Lactic acid-glycolic acid** copolymer  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (rod-like **controlled-release** drug implants)

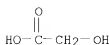
RN 34346-01-5 HCAPLUS

CN Propanoic acid, 2-hydroxy-, polymer with hydroxyacetic acid (9CI) (CA INDEX NAME)

CM 1

CRN 79-14-1

CMF C2 H4 O3



CM 2

CRN 50-21-5  
 CMF C3 H6 O3



L115 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1994:686479 HCAPLUS  
 DN 121:286479  
 ED Entered STN: 10 Dec 1994  
 TI Preparation and characterization of copoly(dL-lactic/  
**glycolic acid**) microparticles for sustained release of  
 thyrotropin releasing hormone by double nozzle spray drying method

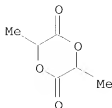
AU Takada, Shigeyuki; Uda, Yoshiaki; Toguchi, Hajime; Ogawa, Yasuaki  
CS DDS Research Laboratories, Takeda Chemical Industries, Ltd. 17-85,  
Juso-honmachi 2-chome, Yodogawa-ku, Osaka, 532, Japan  
SO Journal of Controlled Release (1994), 32(1), 79-85  
CODEN: JCREEC; ISSN: 0168-3659  
DT Journal  
LA English  
CC 63-6 (Pharmaceuticals)  
AB Copoly(dL-lactic/glycolic acid)  
microparticles for sustained release of a water soluble drug (TSH releasing hormone: TRH) were prepared by a spray drying method. In the case of double nozzle spray drying (DNSD) using acetonitrile, the effect of TRH loading amount on the initial burst was smaller than that with in-water drying. The microparticles prepared by DNSD and loaded with up to 10% TRH exhibited a small initial burst followed by a constant release rate over 4 wk. The drug release from the polymer was much faster than the polymer weight loss. The mean particle size of the spray dried microparticles was smaller than that with in-water drying. Acetonitrile used in DNSD is a less toxic organic solvent than dichloromethane, and the residual amount in the microparticles was similar to that in the in-water drying method. In conclusion, the production of biodegradable microparticles by the double nozzle spray drying method should be an attractive alternative to conventional microencapsulation methods.  
ST microparticle injection lactide glycolide copolymer;  
TSH releasing hormone sustained release microparticle; spray drying  
lactide glycolide copolymer microparticle  
IT Particle size  
Solution rate  
(glycolic-dL-lactic acid) microparticles for  
sustained release of TSH releasing hormone by double nozzle spray  
drying method)  
IT Drying  
(spray, (glycolic-dL-lactic acid) microparticles  
for sustained release of TSH releasing hormone by double nozzle spray  
drying method)  
IT Pharmaceutical dosage forms  
(sustained-release, (glycolic-dL-lactic  
acid) microparticles for sustained release  
of TSH releasing hormone by double nozzle spray drying method)  
IT 24305-27-9, Thyrotropin releasing hormone  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(glycolic-dL-lactic acid) microparticles for  
sustained release of TSH releasing hormone by double nozzle spray  
drying method)  
IT 26780-50-7, (Glycolide-DL-lactide copolymer  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(glycolide-DL-lactide) microparticles for  
sustained release of TSH releasing hormone by double nozzle spray  
drying method)  
IT 26780-50-7, (Glycolide-DL-lactide copolymer  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(glycolide-DL-lactide) microparticles for  
sustained release of TSH releasing hormone by double nozzle spray  
drying method)  
RN 26780-50-7 HCAPLUS  
CN 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 1,4-dioxane-2,5-dione  
(9CI) (CA INDEX NAME)  
CM 1  
CRN 502-97-6  
CMF C4 H4 O4





CM 2

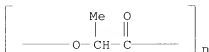
CRN 95-96-5  
CMF C6 H8 O4



L115 ANSWER 10 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN  
AN 1994:331162 HCAPLUS  
DN 120:331162  
ED Entered STN: 25 Jun 1994  
TI Pharmaceutical microspheres for the prolonged release of the LHRH hormone  
and its analogs  
IN Billot, Genevieve B.; Teichner, Marc M.  
PA Rhone-Merieux, Fr.  
SO Can. Pat. Appl., 27 pp.  
CODEN: CPXXEB  
DT Patent  
LA English  
IC ICM A61K037-43  
ICS A61K009-16; A61K009-52; B01J013-02  
CC 63-6 (Pharmaceuticals)  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CA 2100925	AA	19940128	CA 1993-2100925	19930720 <--
	FR 2693905	A1	19940128	FR 1992-9241	19920727 <--
	FR 2693905	B1	19940902		
	AU 9342022	A1	19940210	AU 1993-42022	19930719 <--
	AU 675788	B2	19970220		
	EP 585151	A1	19940302	EP 1993-401874	19930720 <--
	EP 585151	B1	20000105		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	AT 188382	E	20000115	AT 1993-401874	19930720 <--
	ES 2141756	T3	20000401	ES 1993-401874	19930720 <--
	JP 06087758	A2	19940329	JP 1993-204578	19930727 <--
	US 5540937	A	19960730	US 1993-97014	19930727 <--
PRAI	FR 1992-9241	A	19920727 <--		
AB	A process for preparing microspheres for the prolonged release of the LHRH hormone and its analogs is disclosed. Thus, 400 mg poly(DL-lactide-glycolide) was dissolved in 3.5 g of THF and LHRH hormone was gradually added thereto with stirring. The solvent was evaporated and the mass was dissolved in CH2Cl2 and the dispersion was injected into water containing 1% polyvinyl alc. CH2Cl2 was evaporated and microspheres were harvested by filtration, then washed and dried to obtain				

microspheres containing 8.1% LHRH hormone.  
 ST prolonged release pharmaceutical microsphere LHRH hormone  
 IT Solvents  
     (in preparation of prolonged-release pharmaceutical microspheres containing  
 LHRH hormone)  
 IT **Pharmaceutical dosage forms**  
     (microspheres, sustained-release, LHRH hormone in)  
 IT 67-64-1, Acetone, biological studies 67-66-3, Chloroform, biological studies 75-05-8, Acetonitrile, biological studies **75-09-2, Dichloromethane**, biological studies 78-93-3, Methyl ethyl ketone, biological studies 100-51-6, Benzyl alcohol, biological studies 108-88-3, Toluene, biological studies 109-99-9, Thf, biological studies 110-86-1, Pyridine, biological studies 123-91-1, Dioxane, biological studies 141-78-6, Ethyl acetate, biological studies 24980-41-4, Polycaprolactone 25248-42-4, Polycaprolactone **26023-30-3, Poly(lactide)** 26063-00-3, Polyhydroxy butyrate **26100-51-6, Poly(lactic acid)** 26354-94-9, Polyvalerolactone 26680-10-4, **Poly(lactide)** 26744-04-7, Polyhydroxy butyrate **26780-50-7, Poly(glycolide-lactide)** **34346-01-5, Poly(lactic acid-glycolic acid)** 133644-68-5  
 RL: BIOL (Biological study)  
     (in preparation of prolonged-release pharmaceutical microspheres containing hormone)  
 LHRH hormone)  
 IT 9034-40-6, LHRH  
 RL: BIOL (Biological study)  
     (prolonged-release pharmaceutical microspheres containing)  
 IT **75-09-2, Dichloromethane**, biological studies **26023-30-3, Poly(lactide)** **26100-51-6**, **Poly(lactic acid)** **26780-50-7, Poly(glycolide-lactide)** **34346-01-5, Poly(lactic acid-glycolic acid)**  
 RL: BIOL (Biological study)  
     (in preparation of prolonged-release pharmaceutical microspheres containing hormone)  
 LHRH hormone)  
 RN 75-09-2 HCAPLUS  
 CN Methane, dichloro- (8CI, 9CI) (CA INDEX NAME)  
 Cl-CH<sub>2</sub>-Cl  
 RN 26023-30-3 HCAPLUS  
 CN Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] (8CI, 9CI) (CA INDEX NAME)



RN 26100-51-6 HCAPLUS  
 CN Propanoic acid, 2-hydroxy-, homopolymer (9CI) (CA INDEX NAME)

CRN 50-21-5  
CMF C3 H6 O3



RN 26780-50-7 HCAPLUS  
CN 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 1,4-dioxane-2,5-dione  
(9CI) (CA INDEX NAME)

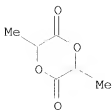
CM 1

CRN 502-97-6  
CMF C4 H4 O4



CM 2

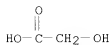
CRN 95-96-5  
CMF C6 H8 O4



RN 34346-01-5 HCAPLUS  
CN Propanoic acid, 2-hydroxy-, polymer with hydroxyacetic acid (9CI) (CA INDEX NAME)

CM 1

CRN 79-14-1  
CMF C2 H4 O3



CM 2

CRN 50-21-5  
CMF C3 H6 O3



L115 ANSWER 11 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1994:307515 HCAPLUS

DN 120:307515

ED Entered STN: 11 Jun 1994

TI Method for producing sustained-release microsphere preparation

IN Kobayashi, Masao; Nishioka, Yukiko; Suzuki, Takehiko; Matsukawa, Yasuhisa

PA Tanabe Seiyaku Co., Ltd., Japan

SO Can. Pat. Appl., 28 pp.

CODEN: CPXXEB

DT Patent

LA English

IC ICM A61K009-52

ICS A61K009-16; A61K009-10; A61K047-34

CC 63-6 (Pharmaceuticals)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CA 2099941	AA	19940117	CA 1993-2099941	19930706 <--
	CA 2099941	C	19991228		
	JP 06032732	A2	19940208	JP 1992-189181	19920716 <--
	JP 2651320	B2	19970910		
	US 5556642	A	19960917	US 1993-89194	19930712 <--
	EP 586838	A1	19940316	EP 1993-111455	19930716 <--
	EP 586838	B1	19971105		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	AT 159854	E	19971115	AT 1993-111455	19930716 <--
	ES 2110544	T3	19980216	ES 1993-111455	19930716 <--
PRAI	JP 1992-189181	A	19920716	<--	

AB A method is disclosed for producing a sustained-release microsphere preparation for a water-soluble medicament which has high incorporation efficiency of the medicament and low initial burst. The method comprises dissolving a water-soluble pharmaceutical active ingredient and a water-insol. biodegradable polymer in 1-2 solvents in which both can dissolve, removing the solvent to give a solid dispersion having the water-soluble pharmaceutical active ingredient dispersed into the biodegradable polymer at a mol. level, and further, dissolving said solid dispersion in an organic solvent being water-immiscible and having a b.p. of <100°C, adding the resulting oil phase into an aqueous phase containing emulsifying agent to give

an oil-in-water emulsion, and removing the organic solvent from the oil phase of the resulting emulsion. The methodol. was applied to preparation of sustained-release microspheres of TRH, a TRH derivative, etc.

ST pharmaceutical sustained release microsphere prepn; TRH sustained release microsphere

IT Solvents

Gelatins, uses

RL: PREP (Preparation)

(in pharmaceutical sustained-release microsphere preparation)

IT Polymers, uses

RL: PREP (Preparation)

(water-insol. in pharmaceutical sustained-release microsphere preparation)

IT Castor oil

RL: PREP (Preparation)

(hydrogenated, ethoxylated, in pharmaceutical sustained-release microsphere preparation)

IT **Pharmaceutical dosage forms**

(**microspheres, sustained-release**, preparation of, solvent dispersion and emulsion formation in)

IT Emulsions  
(oil-in-water, in sustained-release microsphere preparation)

IT 7732-18-5  
RL: BIOL (Biological study)  
(emulsions, oil-in-water, in sustained-release microsphere preparation)

IT 56-23-5, Carbon tetrachloride, uses 64-17-5, Ethanol, uses 67-66-3, Chloroform, uses 75-05-8, Acetonitrile, uses **75-09-2, Methylene chloride**, uses 1300-21-6, Dichloroethane 9002-89-5, Polyvinyl alcohol 9003-39-8, Polyvinylpyrrolidone 25322-68-3, Polyethylene glycol **26023-30-3, Polylactic acid 26100-51-6, Polylactic acid 34346-01-5, Lactic acid-glycolic acid copolymer**  
RL: BIOL (Biological study)  
(in pharmaceutical sustained-release microsphere preparation)

IT 9034-40-6P, LHRH 24305-27-9P, TRH 103300-74-9P 137888-11-0P  
RL: PREP (Preparation)  
(pharmaceutical sustained-release microsphere preparation of)

IT **75-09-2, Methylene chloride**, uses **26023-30-3, Polylactic acid 26100-51-6, Polylactic acid 34346-01-5, Lactic acid-glycolic acid copolymer**  
RL: BIOL (Biological study)  
(in pharmaceutical sustained-release microsphere preparation)

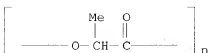
RN 75-09-2 HCAPLUS

CN Methane, dichloro- (8CI, 9CI) (CA INDEX NAME)

Cl-CH<sub>2</sub>-Cl

RN 26023-30-3 HCAPLUS

CN Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] (8CI, 9CI) (CA INDEX NAME)



RN 26100-51-6 HCAPLUS

CN Propanoic acid, 2-hydroxy-, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 50-21-5

CMF C3 H6 O3

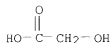


RN 34346-01-5 HCAPLUS

CN Propanoic acid, 2-hydroxy-, polymer with hydroxyacetic acid (9CI) (CA INDEX NAME)

CM 1

CRN 79-14-1  
CMF C2 H4 O3



CM 2

CRN 50-21-5  
CMF C3 H6 O3



L115 ANSWER 12 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1994:280324 HCAPLUS

DN 120:280324

ED Entered STN: 28 May 1994

TI Manufacture of slow-release microcapsules containing pharmaceuticals or agrochemicals

IN Myagawa, Tetsuya; Abe, Seiji; Sakamoto, Izumi

PA Unitika Ltd, Japan

SO Jpn. Kokai Tokkyo Koho, 4 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

IC ICM A61K009-50

ICS A01N025-18; A01N025-28; B01J013-12

CC 63-6 (Pharmaceuticals)

\ Section cross-reference(s): 5

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 06065064	A2	19940308	JP 1992-239012	19920813 <--
PRAI	JP 1992-239012		19920813 <--		

AB Microcapsules that release water-soluble pharmaceuticals (or agrochemicals) slowly for a prolonged period are prepared by forming a water-in-oil emulsion consisting of a water-soluble pharmaceutical (or agrochemicals) solution as internal aqueous phase and then adding this emulsion to an oily polymer solution and drying. For example, a water-in-oil emulsion was prepared (1) by mixing **lactic acid-glycolic acid** copolymer dissolved in **dichloromethane** and an aqueous solution of benzylpenicillin K salt, (2) by adding this emulsion to a poly(vinyl alc.) solution, and (3) finally, by drying the emulsion.

ST microcapsule pharmaceutical agrochem polymer

IT **Encapsulation**

(micro-, of pharmaceuticals and agrochemicals., slow-release)

IT **Pharmaceutical dosage forms**

(slow-release, microencapsulation for)

IT Agrochemical formulations

(sustained-release, microencapsulation for)

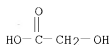
IT 113-98-4, Benzylpenicillin potassium

RL: PROC (Process)

(pharmaceutical microencapsulation of, for slow-release)

IT **34346-01-5, Lactic acid-glycolic**

acid copolymer  
 RL: BIOL (Biological study)  
 (pharmaceutical **microencapsulation** with, for slow-release)  
 IT 34346-01-5, **Lactic acid-glycolic**  
 acid copolymer  
 RL: BIOL (Biological study)  
 (pharmaceutical **microencapsulation** with, for slow-release)  
 RN 34346-01-5 HCAPLUS  
 CN Propanoic acid, 2-hydroxy-, polymer with hydroxyacetic acid (9CI) (CA  
 INDEX NAME)  
 CM 1  
 CRN 79-14-1  
 CMF C2 H4 O3



CM 2  
 CRN 50-21-5  
 CMF C3 H6 O3



L115 ANSWER 13 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1993:525108 HCAPLUS

DN 119:125108

ED Entered STN: 18 Sep 1993

TI Preparations of biodegradable nanospheres of water-soluble and insoluble drugs with **DL-lactide/glycolide** copolymer by a novel spontaneous emulsification solvent diffusion method, and the drug release behavior

AU Niwa, T.; Takeuchi, H.; Hino, T.; Kunou, N.; Kawashima, Y.

CS Dep. Pharm. Eng., Gifu Pharm. Univ., Gifu, 502, Japan

SO Journal of Controlled Release (1993), 25(1-2), 89-98

CODEN: JCREEC; ISSN: 0168-3659

DT Journal

LA English

CC 63-6 (Pharmaceuticals)

AB Nanospheres with **DL-lactide/glycolide** copolymer (PLGA)

were prepared as a biodegradable polymeric carrier for both water-soluble and insol. drugs by a novel spontaneous emulsification solvent diffusion method. Indomethacin and 5-fluorouracil (5-FU) were employed as poorly water-soluble and water-soluble model drugs, resp., to investigate the **encapsulation** efficiency. The drug and PLGA, dissolved in an acetone-dichloromethane (or acetone-chloroform) mixture, were poured into an aqueous solution of polyvinyl alc. with stirring using a high-speed homogenizer when necessary. The dispersed droplets were finely emulsified into nanometer-sized spheres. The marked decrease of the interfacial tension between organic and aqueous phases and the spontaneous

mixing

caused by a rapid diffusion of acetone from the organic to aqueous phase resulted

in the formation of submicron-sized PLGA spheres. The recovery of indomethacin entrapped in the nanospheres (mean diameter: 400-600 nm) increased to 75% at maximum. The rapid deposition of polymeric film on the droplet was required for improving the **encapsulation** of 5-FU to prevent leakage from the droplet. The mean diameter of nanospheres formulated with 5-FU were successfully decreased to 200-300 nm even without high-speed homogenizing. The drug **release** behavior from nanospheres suspended in buffered solution exhibited a biphasic pattern. The initial burst of **release** might be due to the rapid **release** of drugs deposited on the surface and in the water channels of nanospheres. At a later stage, the drug **release** rate was reduced. During the **release** test, PLGA was not degraded for 100 h irrespect of the mol. weight. The mol. weight of polymer was a main factor in **controlling** the drug **release** rate from the nanospheres.

- ST **glycolide lactide polymer controlled release** nanosphere; emulsion solvent diffusion polymer **microencapsulation**
- IT Solution rate  
(of drug, from **glycolide-lactide** nanospheres prepared by emulsion-solvent diffusion method)
- IT Polymer degradation  
Polymer morphology  
(of **glycolide-lactide** copolymer nanospheres)
- IT Particle size  
(of **glycolide-lactide** copolymer nanospheres, conditions during preparation by emulsion-solvent diffusion method effect on)
- IT **Pharmaceutical dosage forms**  
(**controlled-release**, nanospheres, **glycolide-lactide** copolymer, preparation by emulsion-solvent diffusion method and properties of)
- IT **Encapsulation**  
(micro-, with **glycolide-lactide** copolymer, by emulsion-solvent diffusion method)
- IT 67-64-1, Acetone, biological studies 67-66-3, Chloroform, biological studies 75-09-2, Dichloromethane, biological studies 9002-89-5, Poly(vinyl alcohol)  
RL: BIOL (Biological study)  
(in **microencapsulation** with **glycolide-lactides** copolymer by emulsion-solvent diffusion method)
- IT 51-21-8, 5-Fluorouracil 53-86-1, Indomethacin  
RL: PROC (Process)  
(**microencapsulation** of, with **glycolide-lactide** copolymer by emulsion-solvent diffusion method, for **controlled drug release**)
- IT 26780-50-7P, **Glycolide-DL-lactide** copolymer  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(nanospheres, preparation by emulsion-solvent diffusion method of biodegradable, for **controlled drug release**)
- IT 75-09-2, Dichloromethane, biological studies  
RL: BIOL (Biological study)  
(in **microencapsulation** with **glycolide-lactides** copolymer by emulsion-solvent diffusion method)
- RN 75-09-2 HCAPLUS
- CN Methane, dichloro- (8CI, 9CI) (CA INDEX NAME)

CL-CH2-Cl

- IT 26780-50-7P, **Glycolide-DL-lactide** copolymer  
RL: SPN (Synthetic preparation); PREP (Preparation)



(nanospheres, preparation by emulsion-solvent diffusion method of biodegradable, for **controlled drug release**)

RN 26780-50-7 HCAPLUS

CN 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 1,4-dioxane-2,5-dione (9CI) (CA INDEX NAME)

CM 1

CRN 502-97-6

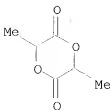
CMF C4 H4 O4



CM 2

CRN 95-96-5

CMF C6 H8 O4



L115 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1993:27476 HCAPLUS

DN 118:27476

ED Entered STN: 24 Jan 1993

TI Swelling agent and biodegradable polymer substances in long-acting pharmaceutical granule preparations

IN Hata, Takehisa; Kagayama, Akira; Kimura, Sumihisa; Ueda, Satoshi; Murata, Saburo

PA Fujisawa Pharmaceutical Co., Ltd., Japan

SO PCT Int. Appl., 20 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

IC ICM A61K009-14

ICS A61K009-22; A61K009-30; A61K047-34

CC 63-6 (Pharmaceuticals)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9216191	A1	19921001	WO 1992-JP318	19920318 <--
	W: JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
EP	576675	A1	19940105	EP 1992-907107	19920318 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	US 5654009	A	19970805	US 1996-635556	19960422 <--
PRAI	JP 1991-132442		19910325		<--
	WO 1992-JP318		19920318		<--

US 1993-117164 19930917 &lt;--

US 1994-320787 19941011 &lt;--

AB A long-acting pharmaceutical granular preparation comprises a core part containing

a drug and a swelling agent and a coating film containing a biodegradable high-mol. substance, wherein the swelling agent is contained in an amount sufficient to burst the coating film after a given period of time. This preparation allows the duration of drug **release** to be **controlled** arbitrarily and is suitable for not only oral administration but also i.m. and s.c. administration. Thus, powder cytarabine 5 g in 20% gelatin solution (520 mL) was made into beads, which were dried, washed and again dried to give 5% cytarabine-containing gelatin beads. The beads were coated with poly(L-lactic acid) in EtOH/dichloromethane. Blood cytarabine level stayed high for a long time after administration.

ST long acting pharmaceutical granule polymer gelatin; cytarabine granule **polylactide** coating

IT Polyesters, biological studies

RL: BIOL (Biological study)

(long-acting pharmaceutical granules coating with)

IT Gelatins, biological studies

RL: BIOL (Biological study)

(long-acting pharmaceutical granules manufacture with)

IT Pharmaceutical dosage forms

(granules, long-acting, swelling agents and biodegradable polymers in)

IT 26063-00-3, Poly-β-hydroxybutyric acid 26161-42-2

26811-96-1 34346-01-5, dl-Lactic acid

glycolic acid copolymer

RL: BIOL (Biological study)

(long-acting pharmaceutical granules coating with)

IT 51-21-8, Fluorouracil 147-94-4, Cytarabine

RL: BIOL (Biological study)

(long-acting pharmaceutical granules containing)

IT 9012-76-4, Chitosan 9067-32-7

RL: BIOL (Biological study).

(long-acting pharmaceutical granules manufacture with)

IT 26161-42-2 34346-01-5, dl-Lactic acid

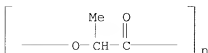
glycolic acid copolymer

RL: BIOL (Biological study)

(long-acting pharmaceutical granules coating with)

RN 26161-42-2 HCAPLUS

CN Poly[oxy[(1S)-1-methyl-2-oxo-1,2-ethanediyl]] (9CI) (CA INDEX NAME)



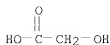
RN 34346-01-5 HCAPLUS

CN Propanoic acid, 2-hydroxy-, polymer with hydroxyacetic acid (9CI) (CA INDEX NAME)

CM 1

CRN 79-14-1

CMF C2 H4 O3



CM 2

CRN 50-21-5  
CMF C3 H6 O3



L115 ANSWER 15 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1992:422904 HCAPLUS

DN 117:22904

ED Entered STN: 26 Jul 1992

TI Efficient microcapsule preparation and method of use

IN Wallace, Sidney; Yang, David J.; Wallace, Michael; Kuang, Li Ren; Li, Chun

PA University of Texas System, USA

SO PCT Int. Appl., 54 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM B01J013-06

CC 9-14 (Biochemical Methods)

Section cross-reference(s): 2, 8, 63

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9205866	A2	19920416	WO 1991-US7366	19911002 <--
	WO 9205866	A3	19920529		
	W: AU, CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
	US 5238714	A	19930824	US 1990-592020	19901002 <--
	CA 2092551	AA	19920403	CA 1991-2092551	19911002 <--
	AU 9190766	A1	19920428	AU 1991-90766	19911002 <--
	AU 659622	B2	19950525		
	EP 553299	A1	19930804	EP 1992-901967	19911002 <--
	EP 553299	B1	19960417		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	JP 06504716	T2	19940602	JP 1992-501033	19911002 <--
	AT 136811	E	19960515	AT 1992-901967	19911002 <--
PRAI	US 1990-592020	A2	19901002 <--		
	WO 1991-US7366	A	19911002 <--		

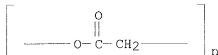
AB A highly efficient method is provided for preparing microcapsules suitable for **encapsulation** or surface attachment of therapeutic or diagnostic agents. In 1 aspect, surface charge of the polymeric material is altered by conjugation of an amino acid ester to the polymer, providing improved targeting of **encapsulated** agents to specific tissue cells. The microcapsules are suitable for attachment of a wide range of targeting agents, including antibodies, steroids, and drugs, which may be attached to the microcapsule polymer before or after formation of suitably sized microcapsules. Microcapsules (1  $\mu\text{m}$ ) loaded with meglumine diatrizoate were prepared using **polylactic acid (PLA)** and PLA conjugated with phenylalanine as the capsular material; the **microencapsulated** diatrizoate was used for bioimaging in rabbits.

- Also described are chemoembolization with e.g, **microencapsulated** cisplatin and the effect of an estrone-poly(benzyl-L-glutamate) conjugate in an in vitro estrogen receptor assay.
- ST microcapsule prepn diagnostic therapeutic; imaging diagnostic microcapsule; meglumine diatrizoate microcapsule **polylactic acid**; phenylalanine **polylactate** conjugate microcapsule diatrizoate; chemoembolization microcapsule cisplatin; estrogen receptor estrone polybenzylglutamate conjugate
- IT Imaging  
(agents for, microcapsule preparation for)
- IT Emulsifying agents  
Sound and Ultrasound  
(in microcapsule preparation for therapeutic or diagnostic)
- IT Polymers, uses  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(in microcapsule preparation for therapeutic or diagnostic)
- IT Therapeutics  
(microcapsule preparation for)
- IT Solvents  
(organic, in microcapsule preparation for therapeutic or diagnostic)
- IT Diagnosis  
(agents, microcapsule preparation for)
- IT Amino acids, compounds  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(conjugates, with polymers, for microcapsule preparation for therapeutic or diagnostic)
- IT Receptors  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(estrogen, microcapsule preparation for therapeutic target agent directed to)
- IT Magnetic substances  
(ferro-, microcapsule preparation for, for diagnostic imaging agent)
- IT Pharmaceutical dosage forms  
(microcapsules, preparation of, for therapeutic or diagnostic)
- IT **Pharmaceutical dosage forms**  
(microcapsules, **sustained-release**, preparation of, for chemoembolization)
- IT Magnetic substances  
(para-, microcapsule preparation for, for diagnostic imaging agent)
- IT Estrogens  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(receptors, microcapsule preparation for therapeutic target agent directed to)
- IT 123-03-5, Cetylpyridinium chloride 151-21-3, Sodium laurylsulfate, uses 1338-39-2, Span 20 9002-89-5, Polyvinyl alcohol 9002-93-1, Triton X-100 9005-65-6, Tween-80 52434-01-2, Lubrol  
RL: ANST (Analytical study)  
(as emulsifier in microcapsule preparation for therapeutic or diagnostic)
- IT 56-23-5, Carbon tetrachloride, uses 67-64-1, 2-Propanone, uses 67-66-3, Chloroform, uses **75-09-2, Methylene chloride**, uses 141-78-6, Acetic acid ethyl ester, uses  
RL: ANST (Analytical study)  
(as solvent in microcapsule preparation for therapeutic or diagnostic)
- IT 142062-09-7  
RL: ANST (Analytical study)  
(estrone-conjugated microcapsules containing, tissue distribution of)
- IT 60-18-4D, L-Tyrosine, polymer conjugates 63-68-3D, Methionine, polymer conjugates 63-91-2D, Phenylalanine, polymer conjugates 73-22-3D, Tryptophan, polymer conjugates  
RL: ANST (Analytical study)  
(for microcapsule preparation for therapeutic or diagnostic)
- IT 1676-73-9 9004-58-4, Ethylhydroxyethyl cellulose 25104-18-1, Polylysine 25248-42-4, Poly[oxy(1-oxo-1,6-hexanediyl)] 25248-42-4D,

- Poly[oxy(1-oxo-1,6-hexanediyl)], diol derivs. **26009-03-0**,  
**Polyglycolic acid** 26099-09-2, Polymaleic acid  
**26100-51-6**, Poly-D,L-lactic acid  
 RL: ANST (Analytical study)  
 (in microcapsule preparation for therapeutic or diagnostic)
- IT **26023-30-3D**, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)],  
 phenylalanine conjugates  
 RL: ANST (Analytical study)  
 (microcapsule prepared with, for diagnostic or therapeutic)
- IT 51-21-8, 5-Fluorouracil 10540-29-1, Tamoxifen 15663-27-1, Cisplatin  
 RL: ANST (Analytical study)  
 (microcapsule preparation for, for chemoembolization)
- IT 131-49-7, Meglumine diatrizoate  
 RL: ANST (Analytical study)  
 (microcapsule preparation for, for diagnostic)
- IT 67-43-6D, DTPA, gadolinium complexes 1949-45-7, Metrizoate 2276-90-6  
 7440-54-2D, Gadolinium, DTPA complexes 59017-64-0 66108-95-0, Iohexol  
 RL: ANST (Analytical study)  
 (microcapsule preparation for, for diagnostic imaging)
- IT 53-16-7, Estrone, biological studies  
 RL: ANST (Analytical study)  
 (microcapsule-attached, microcapsule preparation for, therapeutic directed  
 to estrogen receptor in relation to)
- IT 142062-08-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and reaction of, with polybenzyl-L-glutamate, for microcapsule  
 preparation)
- IT 53-16-7DP, Estrone, polybenzyl-L-glutamate conjugates 25014-27-1DP,  
 estrone conjugates  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of, for microcapsule)
- IT 689-98-5, Chloroethylamine  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reaction of, with estrone)
- IT 63-91-2D, Phenylalanine, esters  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reaction of, with **polylactic acid**, for  
 microcapsule preparation)
- IT **75-09-2, Methylene chloride**, uses  
 RL: ANST (Analytical study)  
 (as solvent in microcapsule preparation for therapeutic or diagnostic)
- RN 75-09-2 HCAPLUS  
 CN Methane, dichloro- (8CI, 9CI) (CA INDEX NAME)

Cl-CH<sub>2</sub>-Cl

- IT **26009-03-0, Polyglycolic acid**  
**26100-51-6, Poly-D,L-lactic acid**  
 RL: ANST (Analytical study)  
 (in microcapsule preparation for therapeutic or diagnostic)
- RN 26009-03-0 HCAPLUS  
 CN Poly[oxy(1-oxo-1,2-ethanediyl)] (9CI) (CA INDEX NAME)



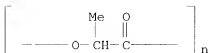
RN 26100-51-6 HCAPLUS  
 CN Propanoic acid, 2-hydroxy-, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 50-21-5  
 CMF C3 H6 O3



IT **26023-30-3D**, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)],  
 phenylalanine conjugates  
 RL: ANST (Analytical study)  
 (microcapsule prepared with, for diagnostic or therapeutic)  
 RN 26023-30-3 HCAPLUS  
 CN Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] (8CI, 9CI) (CA INDEX NAME)



L115 ANSWER 16 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1992:113531 HCAPLUS

DN 116:113531

ED Entered STN: 20 Mar 1992

TI Solvent systems for production of drug microspheres

IN Yamakawa, Ichiro; Machida, Ryoichi; Watanabe, Sumio

PA Eisai Co., Ltd., Japan

SO Eur. Pat. Appl., 12 pp.

CODEN: EPXXDW

DT Patent

LA English

IC ICM A61K009-16

ICS A61K009-51

CC 63-6 (Pharmaceuticals)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 461630	A2	19911218	EP 1991-109610	19910612 <--
	EP 461630	A3	19920401		
	EP 461630	B1	19950913		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	JP 04046115	A2	19920217	JP 1990-152849	19900613 <--
	JP 04046116	A2	19920217	JP 1990-152850	19900613 <--
	JP 06065063	A2	19940308	JP 1991-153830	19910530 <--
	JP 3116311	B2	20001211		
	CA 2044353	AA	19911214	CA 1991-2044353	19910611 <--
	ES 2076412	T3	19951101	ES 1991-109610	19910612 <--
	US 5980947	A	19991109	US 1994-352188	19941201 <--
PRAI	JP 1990-152849	A	19900613 <--		
	JP 1990-152850	A	19900613 <--		
	JP 1991-48579	A	19910222 <--		
	US 1991-713837	B1	19910612 <--		
	US 1993-51272	B1	19930423 <--		

AB Upon incorporation of a drug into microspheres by oil/water solvent

evaporation, a mixed solvent of  $\geq 1$  water-insol. solvent and  $\geq 1$  water-miscible solvent is used as a solvent of an oil phase. The oil phase may also comprise fatty acids or salts thereof, glycerin fatty acid esters, and propylene glycol fatty acid esters. The resulting microspheres contain the drug at a high concentration and slowly **release** from the initial stage after administration. Thus, neurotensin analog 20 and poly(DL-lactic acid) 200 mg were dissolved in 0.6 mL of **methylene chloride**/EtOH (5:1 by volume) and the resulting solution was dispersed in 200 mL of a 0.5 % aqueous solution of PVA.

The

dispersion was stirred for 3 h to conduct oil/water solvent evaporation so that an oil phase was solidified. Microspheres thus formed were collected by a centrifugal separator and lyophilized into powder. The drug content in the microspheres was 21.5 %, vs. 10.4 % for the **control** microspheres produced in a similar manner except that 0.6 mL of **methylene chloride** was used instead of the mixed solvent.

ST microsphere drug solvent system; neurotensin **polylactic acid** drug microsphere

IT Fibrins

RL: BIOL (Biological study)

(enzyme-modified, organic solvent systems containing, in manufacture of drug-containing microspheres)

IT Albumins, biological studies

Gelatins, biological studies

Polyesters, biological studies

RL: BIOL (Biological study)

(organic solvent systems containing, in manufacture of drug-containing microspheres)

IT Collagens, compounds

RL: BIOL (Biological study)

(crosslinked, organic solvent systems containing, in manufacture of drug-containing microspheres)

IT **Pharmaceutical dosage forms**

(**microspheres, sustained-release**, of

water-soluble drugs, solvent systems and additives for manufacture of)

IT Polyethers, biological studies

RL: BIOL (Biological study)

(ortho esters, organic solvent systems containing, in manufacture of drug-containing microspheres)

IT 9002-89-5P, Polyvinyl alcohol

RL: PREP (Preparation)

(emulsifier in manufacture of drug-containing microspheres)

IT 24305-27-9, Thyrotropin-releasing hormone 39379-15-2D, Neurotensin, analogs 74913-18-1D, Dynorphin, analogs

RL: BIOL (Biological study)

(microspheres containing, solvent systems and additives for manufacture of)

IT 108-31-6D, 2,5-Furandione, copolymers 143-18-0, Potassium oleate 143-19-1, Sodium oleate 156-54-7, Sodium butyrate 408-35-5, Sodium palmitate 629-25-4, Sodium laurate 822-12-8, Sodium myristate 822-16-2, Sodium stearate 822-17-3, Sodium linoleate 822-18-4, Sodium linolenate 1002-62-6, Sodium caprate 1002-82-0 1323-39-3, Propylene glycol monostearate 1330-80-9, Propylene glycol monooleate 1984-06-1, Sodium caprylate 3015-50-7 3398-33-2, Sodium undecylenate 4268-61-5, Sodium nonadecanoate 4268-63-7 6106-41-8, Sodium valerate 6610-25-9, Sodium arachidonate 7757-81-5 9003-01-4, Polyacrylic acid 9003-05-8, Polyacrylamide 9003-53-6, Polystyrene 9004-57-3, Ethyl cellulose 10051-44-2, Sodium caproate 10051-45-3 13257-34-6 14047-60-0, Sodium pelargonate 15802-18-3D,  $\alpha$ -Cyanoacrylic acid, esters, polymers 17265-30-4 18175-45-6 25087-26-7, Polymethacrylic acid 25496-72-4,

Glycerin monooleate 26009-03-0, **Glycolic acid**  
 polymer, SRU 26023-30-3, **Lactic acid**  
 polymer, SRU 26023-30-3, Poly(DL-lactic acid  
 ), SRU 26063-00-3, Poly( $\beta$ -hydroxybutyric acid) 26100-51-6  
 , **Lactic acid** polymer 26100-51-6, Poly(DL-  
 lactic acid) 26124-68-5, **Glycolic**  
**acid** polymer 26161-42-2, Poly(L-lactic  
 acid), SRU 26402-22-2, Glycerin monopalmitate 26402-26-6,  
 Glycerin monocaprylate 26657-96-5, Glycerin monopalmitate 26744-04-7,  
 Poly( $\beta$ -hydroxybutyric acid), SRU 26811-96-1, Poly(L- **lactic**  
**acid**) 27194-74-7, Propylene glycol monolaurate 27214-38-6,  
 Glycerin monomyristate 27215-38-9, Glycerin monolaurate 29013-28-3,  
 Propylene glycol monopalmitate 29059-24-3, Propylene glycol  
 monomyristate 31565-12-5, Propylene glycol monocaprylate 31566-31-1,  
 Glycerin monostearate 68795-69-7, Propylene glycol monopalmitate  
 139256-95-4, Sodium isocrotonate  
 RL: BIOL (Biological study)

(organic solvent systems containing, in manufacture of drug-containing microspheres)

IT 56-23-5, biological studies 64-17-5, Ethanol, biological studies  
 67-56-1, Methanol, biological studies 67-63-0, Isopropanol, biological  
 studies 67-66-3, Chloroform, biological studies 67-68-5,  
 Dimethylsulfoxide, biological studies 71-23-8, 1-Propanol, biological  
 studies 75-05-8, Acetonitrile, biological studies 75-09-2,  
**Methylene chloride**, biological studies 110-82-7,  
 Cyclohexane, biological studies 141-78-6, Ethyl acetate, biological  
 studies 1300-21-6, Dichloroethane  
 RL: BIOL (Biological study)

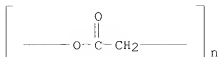
(solvent systems containing, in manufacture of pharmaceutical microspheres)

IT 26009-03-0, **Glycolic acid** polymer, SRU  
 26023-30-3, **Lactic acid** polymer, SRU  
 26100-51-6, **Lactic acid** polymer  
 26124-68-5, **Glycolic acid** polymer  
 26161-42-2, Poly(L-lactic acid), SRU  
 RL: BIOL (Biological study)

(organic solvent systems containing, in manufacture of drug-containing microspheres)

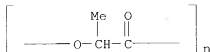
RN 26009-03-0 HCAPLUS

CN Poly[oxy(1-oxo-1,2-ethanediyl)] (9CI) (CA INDEX NAME)



RN 26023-30-3 HCAPLUS

CN Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] (8CI, 9CI) (CA INDEX NAME)



RN 26100-51-6 HCAPLUS

CN Propanoic acid, 2-hydroxy-, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 50-21-5



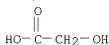
CMF C3 H6 O3



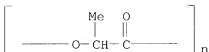
RN 26124-68-5 HCAPLUS  
 CN Acetic acid, hydroxy-, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 79-14-1  
 CMF C2 H4 O3



RN 26161-42-2 HCAPLUS  
 CN Poly[oxy[(1S)-1-methyl-2-oxo-1,2-ethanediyl]] (9CI) (CA INDEX NAME)



IT 75-09-2, **Methylene chloride**, biological studies  
 RL: BIOL (Biological study)  
 (solvent systems containing, in manufacture of pharmaceutical microspheres)  
 RN 75-09-2 HCAPLUS  
 CN Methane, dichloro- (8CI, 9CI) (CA INDEX NAME)

Cl-CH<sub>2</sub>-Cl

L115 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1992:11224 HCAPLUS

DN 116:11224

ED Entered STN: 11 Jan 1992

TI Biocompatible microspheres for the **controlled release**  
 of water-soluble substances and process for preparing them

IN Wantier, Henri; Mathieu, Fabienne; Baudrihay, Marc; Delacroix, Dominique

PA Medgenix Group S. A., Belg.

SO PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DT Patent

LA French

IC ICM B01J013-12

ICS A61K009-52

CC 63-6 (Pharmaceuticals)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9112882	A1	19910905	WO 1991-EP307	19910218 <--

W: CA, JP, US  
 RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE

FR 2658432	A1	19910823	FR 1990-2189	19900222 <--
CA 2053913	AA	19910823	CA 1991-2053913	19910218 <--
CA 2053913	C	20010403		
EP 469110	A1	19920205	EP 1991-903868	19910218 <--
EP 469110	B1	19940727		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 04505420	T2	19920924	JP 1991-503979	19910218 <--
US 5478564	A	19951226	US 1993-77501	19930617 <--
US 5609886	A	19970311	US 1995-507079	19950726 <--

PRAI FR 1990-2189 A 19900222 <--  
 WO 1991-EP307 W 19910218 <--  
 US 1991-768701 B1 19911022 <--  
 US 1991-810403 B1 19911223 <--  
 US 1993-77501 A3 19930617 <--

AB The title comps. comprise a water soluble peptide and a biocompatible and biodegradable polymer **controlling the release** kinetics of the peptide, consisting of a matrix of the polymer within which the water-soluble peptide is evenly dispersed. **Lactic acid-glycolic acid** copolymer was dissolved in CH<sub>2</sub>Cl<sub>2</sub> and mixed with a solution of salmon calcitonin in dimethylacetamide; then the mixture was added to a phosphate buffer containing 4% gelatin. The solvents then evaporated and the emulsion was diluted with water, and filtered to obtain microcapsules of 25-200  $\mu$ m.

ST microcapsule **controlled release** polymer peptide; calcitonin **lactic glycolic** copolymer microcapsule

IT Interferons  
 Peptides, biological studies  
 RL: BIOL (Biological study)  
 (**controlled-release** pharmaceutical microcapsules containing **lactic acid-glycolic acid** copolymer and)

IT Lymphokines and Cytokines  
 RL: BIOL (Biological study)  
 (interleukin 2, **controlled-release** pharmaceutical microcapsules containing **lactic acid-glycolic acid** copolymer and)

IT Lymphokines and Cytokines  
 RL: BIOL (Biological study)  
 (interleukin 4, **controlled-release** pharmaceutical microcapsules containing **lactic acid-glycolic acid** copolymer and)

IT Lymphokines and Cytokines  
 RL: BIOL (Biological study)  
 (interleukin 6, **controlled-release** pharmaceutical microcapsules containing **lactic acid-glycolic acid** copolymer and)

IT **Pharmaceutical dosage forms**  
 (microcapsules, **controlled-release**, of polypeptides containing **lactic acid-glycolic acid** copolymer)

IT Lymphokines and Cytokines  
 RL: BIOL (Biological study)  
 (tumor necrosis factor, **controlled-release** pharmaceutical microcapsules containing **lactic acid-glycolic acid** copolymer and)

IT 64-17-5, Ethanol, biological studies 75-09-2, **Dichloromethane**, biological studies 127-19-5, Dimethylacetamide  
 RL: BIOL (Biological study)  
 (as solvent in preparation of **controlled-release** polypeptide microcapsules)

IT 9002-64-6, PTH 9002-72-6, Growth hormone 9004-10-8, Insulin,

biological studies 9007-12-9, Calcitonin 9007-12-9D, Calcitonin, analogs 9034-39-3, Somatoliberin 9034-40-6, Luteinizing hormone releasing hormone 11096-26-7, Erythropoietin 51110-01-1, Somatostatin 67763-96-6, Insulin-like growth factor I 83869-56-1, Colony-stimulating factor 2 85637-73-6, Atrial natriuretic factor 105913-11-9, Plasminogen activator

RL: BIOL (Biological study)

(**controlled-release** pharmaceutical microcapsules containing **lactic acid-glycolic acid** copolymer and)

IT 34346-01-5, **Lactic acid-glycolic acid** copolymer

RL: BIOL (Biological study)  
(pharmaceutical matrix containing, for **controlled-release** polypeptide microcapsules)

IT 75-09-2, **Dichloromethane**, biological studies

RL: BIOL (Biological study)  
(as solvent in preparation of **controlled-release** polypeptide microcapsules)

RN 75-09-2 HCAPLUS

CN Methane, dichloro- (8CI, 9CI) (CA INDEX NAME)

Cl-CH<sub>2</sub>-Cl

IT 34346-01-5, **Lactic acid-glycolic acid** copolymer

RL: BIOL (Biological study)  
(pharmaceutical matrix containing, for **controlled-release** polypeptide microcapsules)

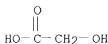
RN 34346-01-5 HCAPLUS

CN Propanoic acid, 2-hydroxy-, polymer with hydroxyacetic acid (9CI) (CA INDEX NAME)

CM 1

CRN 79-14-1

CMF C2 H4 O3



CM 2

CRN 50-21-5

CMF C3 H6 O3



L115 ANSWER 18 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1990:104867 HCAPLUS

DN 112:104867

ED Entered STN: 18 Mar 1990

TI Manufacture of slow-release pharmaceuticals for treatment of Candida infection in the vagina  
 IN Azuma, Seiji; Mitani, Yoko; Suenaga, Fumiyo  
 PA Rohto Pharmaceutical Co., Ltd., Japan  
 SO Jpn. Kokai Tokkyo Koho, 7 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

IC ICM A61K047-00

ICS A61K009-02; A61K009-06; A61K009-70

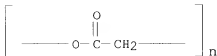
CC 63-6 (Pharmaceuticals)

FAN.CNT 1

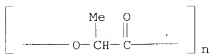
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 01071823	A2	19890316	JP 1987-229251	19870912 <--
PRAI	JP 1987-229251		19870912 <--		
AB	<p>A slow-release pharmaceutical for treatment of Candida infection in the vagina is prepared by dispersing a mixture of pharmaceutical and carrier in a water-soluble polymer. This formulation adheres firmly to the vaginal tissue and releases the pharmaceutical in a controlled manner. Thus, poly(lactic acid) 10, clotrimazole 2, and methylene chloride 100 parts by weight were dissolved, made into a sheet, and pulverized (average particle diameter 100 <math>\mu</math>m). This powder 10 and hydroxypropyl cellulose 10 parts by weight were mixed and made into a rod-shape medication (diam 6 mm and length 3 cm).</p>				
ST	Candida pharmaceutical polymer vagina; fungicide Candida vagina				
IT	Candida				
	(infection with, slow-release pharmaceuticals for treatment of, in vagina)				
IT	Vagina				
	(Candida infection in, slow-release pharmaceuticals for treatment of)				
IT	Fungicides and Fungistats				
	(medical, Candida infection treatment with, in vagina)				
IT	<b>Pharmaceutical dosage forms</b>				
	(slow-release, fungicides and polymers in, for treatment of Candida infection in vagina)				
IT	9000-65-1, Tragacanth gum	9002-89-5, Poly(vinyl alcohol)	9003-01-4, Poly(acrylic acid)	9003-39-8, Polyvinylpyrrolidone	9004-32-4, Carboxymethyl cellulose sodium
	9004-35-7, Cellulose acetate	9004-57-3, Ethyl cellulose	9004-62-0, Hydroxyethyl cellulose	9004-64-2, Hydroxypropyl cellulose	9004-65-3, Hydroxypropyl methyl cellulose
	9004-67-5, Methyl cellulose	9005-37-2, Propylene glycol alginate	9005-38-3, Sodium alginate	9012-76-4, Chitosan	9057-02-7, Pullulan
	11138-66-2, Xanthan gum	25087-26-7, Poly(methacrylic acid)	108188-68-7, 25322-68-3, Polyethylene oxide		
RL:	BIOL (Biological study)				
	(pharmaceutical containing, slow-release, for Candida infection treatment in vagina)				
IT	124-04-9, Adipic acid, biological studies	24980-41-4, Poly( $\epsilon$ -caprolactone)	25248-42-4, Poly[oxy(1-oxo-1,6-hexanediyl)]	26009-03-0, Poly(glycolic acid)	26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)]
	26100-51-6, Poly(lactic acid)	26124-68-5, Poly(glycolic acid)	32474-74-1, Poly(tetramethyl glycolide)	112832-41-4	
RL:	THU (Therapeutic use); BIOL (Biological study); USES (Uses)				
	(pharmaceuticals containing, slow-release, for treatment of Candida infection in vagina)				
IT	1394-02-1, Trichomycin	1397-89-3, Amphotericin B	1400-61-9, Nystatin	7681-93-8, Pimaricin	22916-47-8, Miconazole
	27220-47-9	27523-40-6, Isoconazole	23593-75-1, Clotrimazole		
RL:	BIOL (Biological study)				

(Candida infection treatment with, in vagina)

IT 26009-03-0, Poly(glycolic acid)  
 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)]  
 26100-51-6, Poly(lactic acid)  
 26124-68-5, Poly(glycolic acid)  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (pharmaceuticals containing, slow-release, for treatment of Candida  
 infection in vagina)  
 RN 26009-03-0 HCAPLUS  
 CN Poly[oxy(1-oxo-1,2-ethanediyl)] (9CI) (CA INDEX NAME)



RN 26023-30-3 HCAPLUS  
 CN Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] (8CI, 9CI) (CA INDEX NAME)



RN 26100-51-6 HCAPLUS  
 CN Propanoic acid, 2-hydroxy-, homopolymer (9CI) (CA INDEX NAME)

CM 1

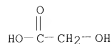
CRN 50-21-5  
 CMF C3 H6 O3



RN 26124-68-5 HCAPLUS  
 CN Acetic acid, hydroxy-, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 79-14-1  
 CMF C2 H4 O3



L115 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1990:84203 HCAPLUS  
 DN 112:84203  
 ED Entered STN: 03 Mar 1990  
 TI Manufacture of slow-release pharmaceutical microgranules  
 IN Machida, Minoru; Arakawa, Masayuki

PA Chugai Pharmaceutical Co., Ltd., Japan  
 SO Jpn. Kokai Tokkyo Koho, 7 pp.  
 CODEN: JKXXAF  
 DT Patent  
 LA Japanese  
 IC ICM A61K009-14  
 ICS A61K047-00  
 CC 63-6 (Pharmaceuticals)  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 01156912	A2	19890620	JP 1988-234758	19880921 <--
	JP 2837675	B2	19981216		
PRAI	JP 1987-236248		19870922 <--		
AB	The title pharmaceuticals contain biodegradable and biocompatible polymers (e.g. <b>polylactic acid</b> ), pharmacol. active substances, and natural polysaccharides (e.g. chitin). The pharmacol. active substances are insol. or sparingly soluble organic compds., proteins, or peptides. Thus, <b>dl-lactic acid-glycolic acid copolymer in methylene chloride</b> -n-propanol was mixed with granulocyte colony-stimulating factor in the same solvent system. To this was added 1% hyaluronic acid to form microspheres (particle size <100 µm).				
ST	slow release pharmaceutical microsphere; colony stimulating factor microsphere; polysaccharide polymer pharmaceutical microsphere				
IT	Polysaccharides, biological studies RL: BIOL (Biological study) (in slow-release pharmaceutical microsphere manufacture)				
IT	Peptides, biological studies Proteins, biological studies RL: BIOL (Biological study) (slow-release pharmaceutical microspheres containing, biodegradable polymers and polysaccharides in)				
IT	<b>Pharmaceutical dosage forms</b> (microgranules, <b>slow-release</b> , biodegradable polymers and polysaccharides in)				
IT	Interferons RL: BIOL (Biological study) (α, slow-release pharmaceutical microspheres containing, biodegradable polymers and polysaccharides in)				
IT	Interferons RL: BIOL (Biological study) (γ, slow-release pharmaceutical microspheres containing, biodegradable polymers and polysaccharides in)				
IT	62683-29-8, Colony-stimulating factor RL: BIOL (Biological study) (granulocyte, slow-release pharmaceutical microspheres containing, biodegradable polymers and polysaccharides in)				
IT	1398-61-4, Chitin 9000-69-5, Pectin 9004-53-9, Dextran 9004-54-0, Dextran, biological studies 9004-61-9, Hyaluronic acid 9007-28-7 9012-76-4, Chitosan 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Poly(dl-lactic acid) 26100-51-6, Polylactic acid 26124-68-5 34346-01-5 52352-27-9, Polyhydroxybutyric acid 122038-63-5 125395-71-3 125395-72-4 RL: BIOL (Biological study) (in slow-release pharmaceutical microsphere manufacture)				
IT	3737-09-5 65141-46-0, Nicorandil RL: BIOL (Biological study) (slow-release pharmaceutical microspheres containing, biodegradable polymers and polysaccharides in)				
IT	26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Poly(dl-lactic acid)				

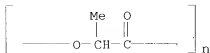
26124-68-5 34346-01-5

RL: BIOL (Biological study)

(in slow-release pharmaceutical microsphere manufacture)

RN 26023-30-3 HCAPLUS

CN Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] (8CI, 9CI) (CA INDEX NAME)



RN 26100-51-6 HCAPLUS

CN Propanoic acid, 2-hydroxy-, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 50-21-5

CMF C3 H6 O3



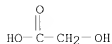
RN 26124-68-5 HCAPLUS

CN Acetic acid, hydroxy-, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 79-14-1

CMF C2 H4 O3



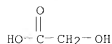
RN 34346-01-5 HCAPLUS

CN Propanoic acid, 2-hydroxy-, polymer with hydroxyacetic acid (9CI) (CA INDEX NAME)

CM 1

CRN 79-14-1

CMF C2 H4 O3



CM 2

CRN 50-21-5

CMF C3 H6 O3



L115 ANSWER 20 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1990:25497 HCAPLUS

DN 112:25497

ED Entered STN: 21 Jan 1990

TI In vitro and in vivo degradation of **poly(DL-lactide/glycolide)** type microspheres made by solvent evaporation method

AU Spenlehauer, G.; Vert, M.; Benoit, J. P.; Boddaert, A.

CS Cent. Rech. Croix de Berny, Rhone-Poulenc Sante, Antony, 92165, Fr.

SO Biomaterials (1989), 10(8), 557-63

CODEN: BIMADU; ISSN: 0142-9612

DT Journal

LA English

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 1, 35, 36

AB Microspheres of different poly( $\alpha$ -hydroxy acids) were prepared by solvent evaporation to study the effects of  $\gamma$ -sterilization on stability and to establish the degradation process in vitro and in vivo.  $\gamma$ -Irradiation dramatically decreases polymer mol. weight and this degradation continues on storage.  $\gamma$ -Irradiation modifies the **controlled-release** pattern of cisplatin-loaded microspheres. After embolization of rat livers by microspheres, a histol. study of the inflammatory response was made, along with gel permeation chromatog. anal. of degrading polymers. The degradation rate of the polymers increased with the glycolic unit content in the **lactic** chains. SEM of microsphere degradation in vitro correlated with the former observations.

ST **polylactide glycolide** microsphere degrdn; gamma irradsn  
**polylactide glycolide** degrdn; sterilization gamma irradsn  
 microsphere degrdn; **controlled release**  
**polylactide glycolide** microsphere

IT Liver

(embolization of, by **poly(lactic acid-co-glycolic acid) controlled-release** microspheres containing cisplatin, polymer degradation in relation to)

IT Sterilization and Disinfection

(gamma-irradiation, of **poly(lactic acid-co-glycolic acid) controlled-release** microspheres, polymer degradation in relation to)

IT Solution rate

(of cisplatin, from **poly(lactic acid-co-glycolic acid) controlled-release** microspheres,  $\lambda$ -irradiation sterilization effect on)

IT Polymer morphology

(**poly(lactic acid-co-glycolic acid) controlled-release** microspheres degradation in relation to)

IT Gamma ray, biological effects

(sterilization by, of **poly(lactic acid-co-glycolic acid) controlled-release** microspheres, polymer degradation in relation to)

IT Polymer degradation

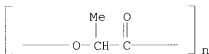
(biochem., of **poly(lactic acid-co-glycolic acid)**, for **controlled-release** microspheres,  $\lambda$ -irradiation sterilization effect on)

IT Embolism

(embolization, of liver, by **poly(lactic acid-co-glycolic acid) controlled-release** microspheres containing cisplatin, polymer degradation in



- relation to)
- IT Polyesters, biological studies  
RL: BIOL (Biological study)  
(glycolic acid-lactic acid, controlled-release microspheres, degradation of,  $\lambda$ -irradiation sterilization effect on)
- IT Polyesters, biological studies  
RL: BIOL (Biological study)  
(lactic acid, controlled-release microspheres, degradation of,  $\lambda$ -irradiation sterilization effect on)
- IT Encapsulation  
(micro-, of cisplatin, by poly(lactic acid-co-glycolic acid), for controlled drug release, solvent evaporation in)
- IT Pharmaceutical dosage forms  
(microspheres, controlled-release, poly(lactic acid-co-glycolic acid), degradation of,  $\lambda$ -irradiation sterilization effect on)
- IT Polymer degradation  
(radiochem., of poly(lactic acid-co-glycolic acid), for controlled-release microspheres, in sterilization)
- IT 26023-30-3 26100-51-6, Poly(DL-lactic acid) 34346-01-5  
RL: BIOL (Biological study)  
(controlled-release microspheres, degradation of,  $\lambda$ -irradiation sterilization effect on)
- IT 15663-27-1, Cisplatin  
RL: BIOL (Biological study)  
(poly(lactide-co-glycolide) controlled-release microspheres containing, degradation of,  $\lambda$ -irradiation sterilization effect on)
- IT 75-09-2, Dichloromethane, uses and miscellaneous  
RL: USES (Uses)  
(solvent, poly(lactic acid-co-glycolic acid) microspheres degradation in relation to residual)
- IT 26023-30-3 26100-51-6, Poly(DL-lactic acid) 34346-01-5  
RL: BIOL (Biological study)  
(controlled-release microspheres, degradation of,  $\lambda$ -irradiation sterilization effect on)
- RN 26023-30-3 HCAPLUS
- CN Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] (8CI, 9CI) (CA INDEX NAME)



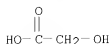
- RN 26100-51-6 HCAPLUS
- CN Propanoic acid, 2-hydroxy-, homopolymer (9CI) (CA INDEX NAME)
- CM 1
- CRN 50-21-5
- CMF C3 H6 O3



RN 34346-01-5 HCAPLUS  
CN Propanoic acid, 2-hydroxy-, polymer with hydroxyacetic acid (9CI) (CA INDEX NAME)

CM 1

CRN 79-14-1  
CMF C2 H4 O3



CM 2

CRN 50-21-5  
CMF C3 H6 O3



IT 75-09-2, Dichloromethane, uses and miscellaneous  
RL: USES (Uses)  
(solvent, poly(lactic acid-co-glycolic acid) microspheres degradation in relation to residual)  
RN 75-09-2 HCAPLUS  
CN Methane, dichloro- (8CI, 9CI) (CA INDEX NAME)



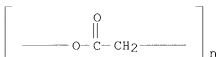
L115 ANSWER 21 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN  
AN 1989:82515 HCAPLUS  
DN 110:82515  
ED Entered STN: 04 Mar 1989  
TI Sustained-release implant for administering growth hormones  
IN Shalati, Mohamad D.; Viswanathan, Ravi  
PA International Minerals and Chemical Corp., USA  
SO U.S., 4 pp.  
CODEN: USXXAM  
DT Patent  
LA English  
IC A61K015-00; A61K021-00; A61K009-22  
ICM A61K009-00  
NCL 424468000  
CC 63-6 (Pharmaceuticals)  
Section cross-reference(s): 2  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4761289	A	19880802	US 1986-917771	19861010 <--
	EP 326727	A1	19890809	EP 1988-300876	19880202 <--
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
PRAI	US 1986-917771		19861010 <--		
AB	The title implants are prepared by dispersing a water-diffusible solid in a solution of a nonaq. solvent and a substantial water-insol. polymer, removing the nonaq. solvent to substantially dry the mixture, comminuting the dry mixture to form particles, and pressing the particles together to form a pellet. Bovine growth hormone (800 mg) was suspended in .apprx.1.7 g CH2Cl2 solution containing 141 mg of <b>poly(lactic acid)</b> (mol. weight 15,600), the solvent evaporated under vacuum at room temperature, 106 mg samples of material pressed into tablets, and the tablets coated with <b>poly(lactic acid)</b> and polycaprolactone.				
ST	sustained release growth hormone implant; bovine growth hormone sustained release				
IT	Epoxy resins, biological studies Polyamides, biological studies Polycarbonates, biological studies Polyesters, biological studies Polysulfones, biological studies Siloxanes and Silicones, biological studies Urethane polymers, biological studies RL: BIOL (Biological study) (sustained-release pellet containing growth hormone and, as implant)				
IT	Ethers, polymers RL: BIOL (Biological study) (alkyl vinyl, polymers, sustained-release pellet containing growth hormone and, as implant)				
IT	<b>Pharmaceutical dosage forms</b> (implants, sustained-release, polymer matrix for)				
IT	Alkenes, polymers RL: BIOL (Biological study) (polymers, chlorosulfonated, sustained-release pellet containing growth hormone and, as implant)				
IT	9004-70-0, Cellulose nitrate RL: BIOL (Biological study) (biocompatible, sustained-release pellet containing growth hormone and, as implant)				
IT	25322-68-3, Polyethylene oxide RL: USES (Uses) (crosslinked, sustained-release pellet containing growth hormone and, as implant)				
IT	<b>75-09-2, Methylene chloride</b> , uses and miscellaneous RL: USES (Uses) (solvent, for sustained-release growth hormone implant pellet manufacture)				
IT	24980-41-4, Polycaprolactone 25248-42-4, Polycaprolactone RL: BIOL (Biological study) (sustained-release pellet containing bioactive protein and, as implant)				
IT	534-15-6 9002-86-2, Polyvinyl chloride 9003-20-7, Polyvinyl acetate 9003-53-6, Polystyrene 9003-54-7, Acrylonitrile styrene copolymer 9004-38-0, Cellulose acetate phthalate 9004-39-1, Cellulose acetate propionate 9012-09-3, Cellulose triacetate 9017-80-5, Polyvinylbenzyltrimethylammonium chloride 9032-35-3, Cellulose acetate succinate 9035-69-2, Cellulose diacetate 9040-62-4, Amylose triacetate 9041-69-4, Cellulose acetate p-toluene sulfonate 24981-14-4, Polyvinyl fluoride 25232-42-2, Polyvinylimidazole <b>26009-03-0</b> , Poly[oxy(1-oxo-1,2-ethanediyl)] <b>26124-68-5</b> , Polyglycolic acid 39382-07-5, Cellulose acetate chloroacetate 62744-35-8,				

Poly(sodium styrene sulfonate) 63340-54-5,  $\beta$ -Glucan triacetate  
 97089-04-8, Cellulose acetate ethyl carbamate 97089-05-9, Cellulose  
 acetate methyl carbamate 116243-80-2 118440-35-0 118440-58-7  
 118440-59-8 118440-60-1 118440-61-2 118441-60-4 118441-64-8  
 RL: BIOL (Biological study)  
 (sustained-release pellet containing growth hormone and, as implant)  
 IT 9004-35-7D, esters, ethers 9004-62-0D, Hydroxyethyl cellulose,  
 acetylated  
 RL: BIOL (Biological study)  
 (sustained-release pellets containing growth hormone and, as implants)  
 IT 9001-63-2, Lysozyme 9002-72-6, Somatotropin 37267-05-3, Ovine growth  
 hormone 66419-50-9, Bovine growth hormone  
 RL: BIOL (Biological study)  
 (sustained-release pellets containing, for implantation)  
 IT 24937-78-8, Ethylene-vinyl acetate copolymer  
 RL: BIOL (Biological study)  
 (sustained-release tablet containing bioactive protein and, as implant)  
 IT 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)]  
 26100-51-6, **Poly(lactic acid)**  
 RL: BIOL (Biological study)  
 (sustained-release tablet containing growth hormone and, as implant)  
 IT 75-09-2, **Methylene chloride**, uses and  
 miscellaneous  
 RL: USES (Uses)  
 (solvent, for sustained-release growth hormone implant pellet manufacture)  
 RN 75-09-2 HCAPLUS  
 CN Methane, dichloro- (8CI, 9CI) (CA INDEX NAME)

Cl-CH<sub>2</sub>-Cl

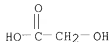
IT 26009-03-0, Poly[oxy(1-oxo-1,2-ethanediyl)] 26124-68-5,  
**Polyglycolic acid**  
 RL: BIOL (Biological study)  
 (sustained-release pellet containing growth hormone and, as implant)  
 RN 26009-03-0 HCAPLUS  
 CN Poly[oxy(1-oxo-1,2-ethanediyl)] (9CI) (CA INDEX NAME)



RN 26124-68-5 HCAPLUS  
 CN Acetic acid, hydroxy-, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 79-14-1  
 CMF C2 H4 O3

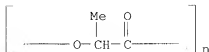


IT 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)]  
 26100-51-6, **Poly(lactic acid)**  
 RL: BIOL (Biological study)

(sustained-release tablet containing growth hormone and, as implant)

RN 26023-30-3 HCAPLUS

CN Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] (8CI, 9CI) (CA INDEX NAME)



RN 26100-51-6 HCAPLUS

CN Propanoic acid, 2-hydroxy-, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 50-21-5

CMF C3 H6 O3



L115 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1988:516065 HCAPLUS

DN 109:116065

ED Entered STN: 01 Oct 1988

TI **Encapsulation** of thyrotropin-releasing hormone or its analog

IN Heya, Toshiro; Okada, Hiroaki; Ogawa, Yasuaki

PA Takeda Chemical Industries, Ltd., Japan

SO Eur. Pat. Appl., 11 pp.

CODEN: EPXXDW

DT Patent

LA English

IC ICM A61K009-52

ICS A61K037-43

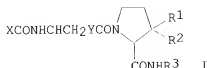
CC 63-6 (Pharmaceuticals)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 256726	A2	19880224	EP 1987-306794	19870731 <--
	EP 256726	A3	19880420		
	EP 256726	B1	19921007		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	JP 63233926	A2	19880929	JP 1987-173523	19870710 <--
	JP 2526589	B2	19960821		
	CA 1300011	A1	19920505	CA 1987-543516	19870731 <--
	AT 81288	E	19921015	AT 1987-306794	19870731 <--
	FI 8800511	A	19890111	FI 1988-511	19880204 <--
	NO 8800502	A	19890111	NO 1988-502	19880204 <--
	HU 52700	A2	19900828	HU 1988-530	19880204 <--
	HU 203479	B	19910828		
	US 5652220	A	19970729	US 1995-416518	19950404 <--
PRAI	JP 1986-187467		19860808	<--	
	JP 1987-173523		19870710	<--	
	US 1987-73741		19870715	<--	
	EP 1987-306794		19870731	<--	
	US 1989-332373		19890403	<--	
	US 1992-882255		19920508	<--	
	US 1993-62144		19930517	<--	

OS MARPAT 109:116065

GI



AB Microcapsules containing polymers and TRH analogs (I; X = 4-, 5-, or 6-membered heterocyclic group; Y = imidazol-4-yl, 4-hydroxyphenyl; R1, R2 = H, lower alkyl; R3 = H, optionally substituted aralkyl) and their salts, are prepared to achieve a sustained-release of the active ingredients. TRH dissolved in water was added to a solution of **lactic acid** **-glycolic acid** copolymer in dichloromethane to give a TRH concentration at 2.5-15 % by weight relative to the copolymer and the

mixture was stirred. The emulsion thus obtained was cooled to 18°, poured to an aqueous solution of PVA and the whole was mixed to give a water/oil/water emulsion. The internal water/oil emulsion was allowed to solidify by evaporating the solvent and the solid phase was dispersed in water. The microcapsules collected were freeze-dried and subjected to tests for the measurement of drug trapping rate and dissoln. rate; the drug trapping rate for the microcapsules containing TRH at 7.5 % by weight relative to the copolymer was 95.9% and initial drug release was 8.8%.

ST microcapsule TSH releasing hormone polymer

IT Gelatins, biological studies

RL: BIOL (Biological study)

(dispersing agent in emulsification for **microencapsulation** of peptides)

IT Fatty acids, esters

RL: BIOL (Biological study)

(esters, polymers, sustained-release pharmaceutical capsules containing peptides and)

IT **Pharmaceutical dosage forms**

(**microcapsules, sustained-release**, of peptides, polymers in)

IT Polyethers, biological studies

RL: BIOL (Biological study)

(ortho esters, sustained-release pharmaceutical capsules containing peptides and)

IT 9002-89-5, Polyvinyl alcohol 9004-32-4, Carboxymethyl cellulose

RL: BIOL (Biological study)

(dispersing agent in emulsification for **microencapsulation** of peptides)

IT 24305-27-9, TRH 25575-91-1 62305-86-6, CG 3509 77026-81-4, DN 1417

RL: BIOL (Biological study)

(sustained-release microcapsules of, polymers in)

IT **34346-01-5, Glycolic acid-lactic acid** copolymer

RL: BIOL (Biological study)

(sustained-release pharmaceutical capsules containing peptides and)

IT **34346-01-5, Glycolic acid-lactic acid** copolymer

RL: BIOL (Biological study)

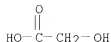
(sustained-release pharmaceutical capsules containing peptides and)

RN 34346-01-5 HCAPLUS

CN Propanoic acid, 2-hydroxy-, polymer with hydroxyacetic acid (9CI) (CA INDEX NAME)

CM 1

CRN 79-14-1  
CMF C2 H4 O3



CM 2

CRN 50-21-5  
CMF C3 H6 O3



L115 ANSWER 23 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1986:74936 HCAPLUS

DN 104:74936

ED Entered STN: 08 Mar 1986

TI Preparation of injectable **controlled-release**  
microcapsules by a solvent-evaporation process

AU Tice, Thomas R.; Gilley, Richard M.

CS Microencapsulation Div., South. Res. Inst., Birmingham, AL, 35255-5305,  
USA

SO Journal of Controlled Release (1985), 2, 343-52

CODEN: JCREEC; ISSN: 0168-3659

DT Journal

LA English

CC 63-5 (Pharmaceuticals)

AB Solvent-evaporation is useful for the **microencapsulation** of water-soluble and water-insol. drugs. The process consists of dissolving a water-insol. drug and a polymer in a volatile organic solvent which is immiscible with water and has a b.p. less than that of water, and adding the organic phase to water containing a dispersing agent. The resulting oil-in-water emulsion contains the drug, polymer and solvent in the oil phase. A vacuum is then slowly applied to the stabilized emulsion to remove the volatile solvent. The microcapsules formed after the removal of the solvent are hard, can be isolated by centrifugation and drying. The product is a free-flowing powder consisting of spherical particles. The rate of solvent evaporation should not be too fast as this will disrupt the walls of the microcapsules. The process is suitable for preparing microcapsules <1 µm (for i.v. administration) and for those <100 µg (for i.m. or s.c. administration). Some examples of the drugs **microencapsulated** by polymers are given.

ST **controlled release** microcapsule; solvent evapn  
**microencapsulation**

IT Albumins

RL: BIOL (Biological study)

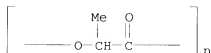
(**controlled-release** microcapsules, formation of, by  
solvent-evaporation)

IT Evaporation

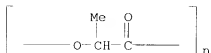
(in preparation of **controlled-release** microcapsules for  
injections)

IT **Encapsulation**

(micro-, of drugs, by polymers, solvent-evaporation method in)  
IT Capsules, pharmaceutical  
(micro-, **controlled-release**, solvent evaporation methods  
for manufacture of injectable)  
IT 25038-32-8 26023-30-3 26161-42-2 26680-10-4  
26780-50-7 33135-50-1  
RL: BIOL (Biological study)  
(**controlled-release** microcapsules, formation of, by  
solvent-evaporation)  
IT 75-09-2, biological studies  
RL: BIOL (Biological study)  
(in **microencapsulation** of drugs by evaporation)  
IT 57-85-2 68-22-4  
RL: BIOL (Biological study)  
(**microencapsulation** of, by polymers, solvent-evaporation method  
in)  
IT 26023-30-3 26161-42-2 26780-50-7  
RL: BIOL (Biological study)  
(**controlled-release** microcapsules, formation of, by  
solvent-evaporation)  
RN 26023-30-3 HCAPLUS  
CN Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] (8CI, 9CI) (CA INDEX NAME)



RN 26161-42-2 HCAPLUS  
CN Poly[oxy[(1S)-1-methyl-2-oxo-1,2-ethanediyl]] (9CI) (CA INDEX NAME)



RN 26780-50-7 HCAPLUS  
CN 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 1,4-dioxane-2,5-dione  
(9CI) (CA INDEX NAME)

CM 1

CRN 502-97-6

CMF C4 H4 O4

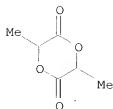


CM 2

CRN 95-96-5

CMF C6 H8 O4





IT 75-09-2, biological studies  
 RL: BIOL (Biological study)  
 (in **microencapsulation** of drugs by evaporation)  
 RN 75-09-2 HCAPLUS  
 CN Methane, dichloro- (8CI, 9CI) (CA INDEX NAME)

Cl-CH<sub>2</sub>-Cl

=> => fil wpix

FILE 'WPIX' ENTERED AT 10:59:26 ON 09 FEB 2004  
 COPYRIGHT (C) 2004 THOMSON DERWENT

FILE LAST UPDATED: 5 FEB 2004 <20040205/UP>  
 MOST RECENT DERWENT UPDATE: 200409 <200409/DW>  
 DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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>>> SLART (Simultaneous Left and Right Truncation) is now  
 available in the /ABEX field. An additional search field  
 /BIX is also provided which comprises both /BI and /ABEX <<<

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 PLEASE VISIT:  
[http://www.stn-international.de/training\\_center/patents/stn\\_guide.pdf](http://www.stn-international.de/training_center/patents/stn_guide.pdf) <<<

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>>> ADDITIONAL POLYMER INDEXING CODES WILL BE IMPLEMENTED FROM  
 DERWENT UPDATE 200403.  
 THE TIME-RANGE CODE WILL ALSO CHANGE FROM 018 TO 2004.  
 SDIS USING THE TIME RANGE CODE WILL NEED TO BE UPDATED.  
 FOR FURTHER DETAILS: <http://thomsonderwent.com/chem/polymers/> <<<

=> d all abeq tech abex tot 1137

L137 ANSWER 1 OF 3 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN  
 AN 2003-615263 [58] WPIX  
 CR 1991-295351 [40]; 1995-199683 [26]; 1996-019737 [02]; 1997-393337 [36];  
 1998-031704 [03]; 1998-129287 [12]; 1998-347245 [30]; 1998-437043 [37];

2001-396353 [42]; 2003-101718 [09]; 2003-730422 [69]  
DNN N2003-489883 DNC C2003-167740  
TI Preparation of controlled released microcapsule formulation comprises dissolving drug and mixture of **uncapped** and **end-capped** biocompatible polymer in organic solvent and evaporating solvent.  
DC A23 A96 B05 B07 P32  
IN SETTERSTROM, J A; VAN HAMONT, J E; VAUGHN, W M  
PA (USSA) US SEC OF ARMY  
CYC 1  
PI US 6528097 B1 20030304 (200358)\* 16p A61K009-50 <--  
ADT US 6528097 B1 Cont of US 1984-590308 19840316, CIP of US 1995-446149  
19950522, Div ex US 1996-675895 19960705, US 2000-716856 20001120  
FDT US 6528097 B1 Div ex US 6217911  
PRAI US 1996-675895 19960705; US 1984-590308 19840316; US 1995-446149  
19950522; US 2000-716856 20001120  
IC ICM **A61K009-50**  
ICS A61F013-00; A61K031-19  
AB US 6528097 B UPAB: 20031027  
NOVELTY - Preparation of controlled release microcapsule formulation comprises:  
(I) dissolving a non-steroidal, anti-inflammatory drug and a mixture of **uncapped** biocompatible, biodegradable poly(lactide/glycolide) polymer and **end-capped** biocompatible, biodegradable poly(lactide/glycolide) polymer in an organic solvent;  
(II) dispersing the dissolved mixture; and  
(III) evaporating the solvent.  
DETAILED DESCRIPTION - Preparation of controlled release microcapsule formulation for programmable release of non-steroidal anti-inflammatory drug comprises either:  
(1) Process A:  
(a) dissolving a non-steroidal, anti-inflammatory drug and a mixture of **uncapped** biocompatible, biodegradable poly(lactide/glycolide) polymer and **end-capped** biocompatible, biodegradable poly(lactide/glycolide) polymer in a volatile organic solvent;  
(b) dispersing the dissolved mixture in an aqueous phase containing emulsion stabilizer; and  
(c) evaporating the organic solvent phase to obtain non-steroidal anti-inflammatory drug loaded microsphere; or  
(2) Process B:  
(a) dissolving a non-steroidal, anti-inflammatory drug and a mixture of **uncapped** biocompatible, biodegradable poly(lactide/glycolide) polymer and **end-capped** biocompatible, biodegradable poly(lactide/glycolide) polymer in an polar organic solvent;  
(b) dispersing the dissolved drug in a non-polar organic phase;  
(c) pouring the emulsion into a hydrocarbon solvent; and  
(d) extracting the polar organic phase into the hydrocarbon solvent to form microsphere.  
An INDEPENDENT CLAIM is also included for the preparation of a controlled release microcapsule formulation for programmable release of a long acting local anesthetic comprising:  
(A) dissolving long-acting local anesthetic and a mixture of **uncapped** biocompatible, biodegradable poly(lactide/glycolide) polymer and **end-capped** biocompatible, biodegradable poly(lactide/glycolide) polymer in a volatile organic solvent;  
(B) dispersing the local anesthetic and volatile organic solvent in an aqueous phase containing emulsion stabilizer; and  
(C) evaporating the volatile organic solvent to precipitate microspheres of local anesthetic and poly(lactide/

**glycolide) microspheres.**

ACTIVITY - Analgesic; Antiarthritic.

MECHANISM OF ACTION - None given.

USE - For preparing a controlled release microcapsule formulation (claimed) for drugs, e.g. non-steroidal antiinflammatory drug; for treating pain, arthritis.

ADVANTAGE - The composition is burst free and has sustained programmable release of drugs. The drug is evenly distributed through poly(lactide/glycolide) matrix.

Dwg.0/10

FS CPI GMPI

FA AB; DCN

MC CPI: A05-E02; A08-S02; A09-A07; A10-E01; A12-V01; B04-C03D; B07-D05; B10-B01A; B10-B02A; B10-B02F; B10-C03; B10-C04B; B10-C04C; B10-D03; B12-M10A; B12-M11E; B14-C03; B14-C08

TECH UPTX: 20030910

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: The non-steroidal anti-inflammatory drug is selected from ibuprofen, florbipirofen (sic), aspirin, acetaminophen, endocen (sic), toridol (sic), voltren (sic), telecten (sic) and ketoprofen (preferably ketoprofen).

The drug comprises a homogenous solid matrix.

The local anesthetic is selected from tetracaine, lidocaine, etidocaine, carbocaine (sic), xylocaine, marcaine, nesacaine and etiod (preferably lidocaine).

TECHNOLOGY FOCUS - POLYMERS - Preferred Components: The biodegradable poly(lactide/glycolide) polymer comprises a ratio of lactide to glycolide 100:0 - 50:50 and have a molecular weight of 10-100 kDa.

The **end-capped** polymer is hydrophobic and comprises terminal residues functionalized as esters.

The **uncapped** polymer is hydrophilic and comprises terminal residues existing as carboxylic acid.

Polymer comprises a homogenous solid matrix.

ABEX UPTX: 20030910

SPECIFIC COMPOUNDS - The non-steroidal anti-inflammatory drug is ibuprofen, florbipirofen (sic), aspirin, acetaminophen, endocen (sic), toridol (sic), voltren (sic), telecten (sic) and ketoprofen.

The local anesthetic is tetracaine, lidocaine, etidocaine, carbocaine (sic), xylocaine, marcaine, nesacaine and etiod.

ADMINISTRATION - The composition is administered locally (claimed) or systemically.

EXAMPLE - Ketoprofen and poly(DL-lactide-co-glycolide)

(PLGA) were dissolved in **methylene chloride** and

dispersed in an aqueous phase containing an emulsion stabilizer.

Evaporation of the organic phase gave ketoprofen-loaded microspheres. The microspheres released ketoprofen for 2 weeks to 2 months with minimal burst release.

L137 ANSWER 2 OF 3 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

AN 1998-437043 [37] WPIX

CR 1991-295351 [40]; 1995-199683 [26]; 1996-019737 [02]; 1997-393337 [36];

1998-031704 [03]; 1998-129287 [12]; 1998-347245 [30]; 2001-396353 [42];

2003-101718 [09]; 2003-615263 [58]; 2003-730043 [69]; 2003-730422 [69]

DNC C1998-132804

TI New burst-free, sustained, programmable release composition(s) - containing an active material in a blend of **uncapped** and **end-capped** co polymer, preferably a poly (DL-lactide-co glycolide).

DC A96 B04 B05 B07 D16 P73

IN BOEDEKER, E C; BROWN, W; CASSELS, F; FRIDEN, P; JACOB, E; JARBOE, D L;  
 JEYANTHI, R; MCQUEEN, C E; REID, R H; ROBERTS, F D; SETTERSTROM, J A;  
 THIES, C; TICE, T R; VAN HAMONT, J E  
 PA (USSA) US SEC OF ARMY  
 CYC 79  
 PI WO 9832427 A1 19980730 (199837)\* EN 422p A61K009-52 <--  
 RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA  
 PT SD SE SZ UG ZW  
 W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE  
 GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW  
 MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN  
 YU ZW  
 AU 9863175 A 19980818 (199851)  
 US 6309669 B1 20011030 (200172) A61K009-52 <--  
 US 6410056 B1 20020625 (200246)# A61K009-50 <--  
 ADT WO 9832427 A1 WO 1998-US1556 19980127; AU 9863175 A AU 1998-63175  
 19980127; US 6309669 B1 Cont of US 1984-590308 19840306, CIP of US  
 1984-590308 19840316, CIP of US 1992-867301 19920410, CIP of US  
 1995-446148 19950522, CIP of US 1995-446149 19950522, CIP of US  
 1996-590973 19960124, US 1997-789734 19970127; US 6410056 B1 CIP of US  
 1984-590308 19840316, CIP of US 1990-493597 19900315, CIP of US  
 1994-209350 19940107, US 1995-446148 19950522  
 FDT AU 9863175 A Based on WO 9832427; US 6309669 B1 CIP of US 5417986  
 PRAI US 1997-789734 19970127; US 1984-590308 19840306; US 1992-867301  
 19920410; US 1995-446148 19950522; US 1995-446149 19950522; US  
 1996-590973 19960124  
 IC ICM A61K009-50; A61K009-52  
 ICS A61K047-30; B32B005-16  
 AB WO 9832427 A UPAB: 20031027

A composition is claimed for the burst-free, sustained, programmable release of active material(s) over a period from 1-100 days, comprising: (a) an active material; and (b) a carrier which may contain pharmaceutically-acceptable adjuvant, comprised of a blend of **uncapped and end-capped** biodegradable-biocompatible copolymer.

Also claimed are: (1) a process for preparing controlled release compositions characterised by burst-free, sustained, programmable release of biologically active agents, comprising: (a) dissolving biodegradable poly(lactide/glycolide), in **uncapped or end-capped form in methylene chloride**, and dissolving a biologically active agent or active core in water; (b) adding the aqueous layer to the polymer solution and emulsifying to provide an inner water-in-oil (w/o) emulsion; (c) stabilising the w/o emulsion in a solvent-saturated aqueous phase containing an oil-in-water (o/w) emulsifier; (d) adding the w/o emulsion to an external aqueous layer containing o/w emulsifier to form a ternary emulsion; and (e) stirring the resulting water-in-oil-in-water (w/o/w) emulsion to remove the solvent, and rinsing hardened microcapsules with water and lyophilising the hardened microcapsules; (2) a method for the protection against infection of a mammal by pathogenic organisms comprising administering orally to the mammal an immunogenic amount of an immunostimulating composition consisting of an antigenic synthetic peptide encapsulated within a poly(lactide/galactide) matrix; (3) a vaccine for the immunisation of a mammal against infection by pathogenic organisms consisting of an antigen in an amount of 0.1-1% encapsulated within a biodegradable-biocompatible polymeric poly(DL-lactide-co-glycolide) matrix where the polymer is **end-capped** or a blend of **uncapped and end-capped** polymers; and (4) an immunostimulating composition comprising encapsulating-microspheres, which may contain an adjuvant, where the microspheres having a diameter of 1 nm to 10 microns are comprised of: (a) a biodegradable-biocompatible poly (DL-lactide-co-glycolide) as the bulk matrix, where the copolymer (

**lactide to glycolide L/G) ratio for uncapped and end-capped polymer is 0/100 to 1/99; and (b) an immunogenic substance comprising a bacteria, virus, fungus, parasite, or derivative, that serves to elicit the production of antibodies in animal subjects.**

USE - The biocompatible and biodegradable microspheres can provide programmable sustained release of biologically active agents, including polypeptides over a period of up to 100 days in an aqueous physiological environment with little or no burst release. They can be used for the delivery of e.g. insulins, AZT, diethyl silbestrol, 17-beta-oestradiol, oestron, ethinyl estradiol, mestranol, norethindrone, norgestryl, ethynodiol diacetate, lynoestrenol, medroxyprogesterone acetate, dimethisterone, megestrol acetate, chlormadinine acetate, norgestimate, norethisterone, ethisterone, melentate, norgestimate, norethisterone, ethisterone, melentate, melengestrol, norethynodrel, nonylphenoxypolyoxyethylene glycol, benzethonium chloride, chlorindanol, aluminium hydroxide, calcium carbonate, magnesium carbonate, sodium carbonate, chlorpromazine HCl, clozapine, mesoridazine, metiapine, reserpine, thioridazine, chlordiazepoxide, diazepam, meprobamate, temazepam, codeine, phenobarbital, sodium pentobarbital, sodium secobarbital, testosterone, testosterone propionate, sulphonamides, 4-aminoquinolines, 8-aminoquinolines, pyrimethamine, mazingol, phentermine, L-dopa, atropine, methscopolamine bromide, dextromethorphan, noscapine, Rauwolfia alkaloids, nitroglycerin, organic nitrites, pentaerythritotetranitrate, potassium chloride, ergotamine with and without caffeine, hydrogenated ergot alkaloids, dihydroergocristine methanesulphate, dihydroergocornine methanesulphonate, dihydroergokryptine methanesulphate, atropine sulphate, Belladonna, hyoscyne hydrobromide, dihydrocodienone, meperidine, morphine, salicylates, aspirin, acetaminophen, d-propoxyphene, ceflacor, cefuroxime, chloramphenicol, gentamycin, Kanamycin A, Kanamycin B, ampicillin, amoxicillin, streptomycin A, antimonycin A, chloropamtheniol, metromidazole, oxytetracycline, penicillin G, minocycline, ciprofloxacin, ofloxacin, clarithromycin, erythromycin (sic), gentamicin, amikacin, tobramycin, kanamycin, ampicillin, polymyxin-B, amphotericin-B, aztrofonam, chloramphenicol, fusidans, lincosamides, metronidazole, nitro-furantion, imipenem/cilastin, quinolones, rifampin, polyenes, sulphonamides, trimethoprim, vancomycin, teicoplanin, imidazoles, mephenytoin, phenobarbital, trimethadione, triethylperazine, chlorophenazine, dimenhydrinate, diphenhydramine, perphenazine, tripeleminamine, hydrocortisone, prednisolone, prednisone, allopurinol, indomethacin, phenylbutazone, prostaglandin, thiotepa, chloramucil, cyclophosphamide, melphalan, nitrogen mustard, methotrexate, aztreonam, and refampin.

Dwg.0/54

FS CPI GMP1

FA AB; DCN

MC CPI: A05-E02; A10-E01; A12-V01; B02-P03; B04-B04C; B04-C03D; B04-F09; B04-F10; B04-F11; **B12-M10A; B12-M11E**; B14-G01; B14-S11; D05-H07

L137 ANSWER 3 OF 3 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

AN 1997-393337 [36] WPIX

CR 1991-295351 [40]; 1995-199683 [26]; 1996-019737 [02]; 1998-031704 [03];

1998-129287 [12]; 1998-347245 [30]; 1998-437043 [37]; 2001-396353 [42];

2003-101718 [09]; 2003-615263 [58]; 2003-730043 [69]; 2003-730422 [69]

DNC C1997-126303

TI Microcapsule compositions for burst-free, sustained release of active agents - comprising active agent and blend of **uncapped and end-capped** biodegradable poly(lactide/glycolide).

DC A23 A25 A96 B04 B07

IN FRIDEN, P; JEYANTHI, R; MCQUEEN, C E; REID, R H; ROBERTS, F D; SETTERSTROM, J A; VAN HAMONT, J F

PA (USSA) US SEC OF ARMY

CYC 71

PI WO 9726869 A1 19970731 (199736)\* EN 52p A61K009-50 <--  
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 SE SZ UG  
 W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS  
 JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT  
 RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN  
 AU 9714104 A 19970820 (199749)  
 EP 817619 A1 19980114 (199807) EN  
 R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE  
 NZ 325561 A 19990629 (199931) A61K009-50 <--  
 JP 11509862 W 19990831 (199946) 40p A61K009-52 <--  
 KR 98703429 A 19981105 (199954)  
 MX 9707310 A1 19980601 (200009)  
 BR 9607752 A 19991130 (200014)  
 AU 722884 B 20000810 (200043)  
 NZ 335409 A 20001222 (200104) A61K009-52 <--  
 CN 1188408 A 19980722 (200270) A61K009-50 <--  
 ADT WO 9726869 A1 WO 1996-US19440 19961118; AU 9714104 A AU 1997-14104  
 19961118; EP 817619 A1 EP 1996-944247 19961118, WO 1996-US19440 19961118;  
 NZ 325561 A NZ 1996-325561 19961118, WO 1996-US19354 19961118; JP 11509862  
 W WO 1996-US19440 19961118, JP 1997-526833 19961118; KR 98703429 A WO  
 1996-US19440 19961118, KR 1997-706833 19970924; MX 9707310 A1 MX 1997-7310  
 19970924; BR 9607752 A BR 1996-7752 19961118, WO 1996-US19440 19961118; AU  
 722884 B AU 1997-14104 19961118; NZ 335409 A Div ex NZ 1996-325561  
 19961118, NZ 1996-335409 19961118; CN 1188408 A CN 1996-194768 19961118  
 FDT AU 9714104 A Based on WO 9726869; EP 817619 A1 Based on WO 9726869; NZ  
 325561 A Based on WO 9726869; JP 11509862 W Based on WO 9726869; KR  
 98703429 A Based on WO 9726869; BR 9607752 A Based on WO 9726869; AU  
 722884 B Previous Publ. AU 9714104, Based on WO 9726869; NZ 335409 A Div  
 ex NZ 325561  
 PRAI US 1996-590973 19960124  
 REP US 4622244; US 4623588  
 IC ICM A61K009-50; A61K009-52  
 ICS A61K038-08; A61K038-09; A61K038-10; A61K047-30  
 AB WO 9726869 A UPAB: 20031027

The following are claimed: (A) a controlled release microcapsule pharmaceutical formulation, for burst-free, sustained, programmable release of a biologically active agent over 1-100 days, comprising an active agent and a blend of uncapped and end-capped biodegradable poly(lactide/glycolide) (PLG). (B) preparing controlled release microcapsule formulations characterised by burst-free, sustained, programmable release of biologically active agents, comprising: (a) dissolving biodegradable PLG, in uncapped or end-capped form, in methylene chloride, and dissolving an active agent or active core in water; (b) adding the aqueous layer to the polymer solution and emulsifying to provide an inner water-in-oil emulsion; (c) stabilising the emulsion in a solvent-saturated aqueous phase containing an oil-in-water emulsifier; (d) adding the water-in-oil emulsion to an external aqueous layer containing oil-in-water emulsifier to form a ternary emulsion; and (e) stirring the resulting water-in-oil-in-water emulsion for sufficient time to remove the solvent, rinsing the hardened microcapsules with water, and lyophilising the microcapsules.

USE - The microcapsules are useful for sustained, burst-free, release of active agents, e.g., polypeptides, over long periods of time.

ADVANTAGE - The microcapsules show high encapsulation efficiency. The carrier polymer is completely degraded to innocuous components. The microcapsules are easily administered via, e.g., oral, parenteral, topical, nasal or vaginal routes.

Dwg.0/7

FS CFI

FA AB; DCN  
 MC CPI: A05-E02; A07-A03A; A09-A07; A12-V01; **B12-M11E**

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 PATENTS CITATION INDEX, COVERS 1973 TO DATE

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L142 ANSWER 1 OF 6 DPCI COPYRIGHT 2004 THOMSON DERWENT on STN  
 AN 2003-615263 [58] DPCI  
 CR 1991-295351 [40]; 1995-199683 [26]; 1996-019737 [02]; 1997-393337 [36];  
 1998-031704 [03]; 1998-129287 [12]; 1998-347245 [30]; 1998-437043 [37];  
 2001-396353 [42]; 2003-101718 [09]; 2003-730422 [69]  
 DNN N2003-489883 DNC C2003-167740  
 TI Preparation of controlled released microcapsule formulation comprises  
 dissolving drug and mixture of uncapped and end-capped biocompatible  
 polymer in organic solvent and evaporating solvent.  
 DC A23 A96 B05 B07 P32  
 IN SETTERSTROM, J A; VAN HAMONT, J E; VAUGHN, W M  
 PA (USSA) US SEC OF ARMY  
 CYC 1  
 PI US 6528097 B1 20030304 (200358)\* 16p A61K009-50  
 ADT US 6528097 B1 Cont of US 1984-590308 19840316, **CIP of US 1995-446149**  
**19950522**, Div ex US 1996-675895 19960705, US 2000-716856 20001120  
 FDT US 6528097 B1 Div ex US 6217911  
 PRAI US 1996-675895 19960705; US 1984-590308 19840316; US 1995-446149  
 19950522; US 2000-716856 20001120  
 IC ICM A61K009-50  
 ICS A61F013-00; A61K031-19  
 FS CPI GMP1

EXF EXAMINER'S FIELD OF SEARCH UPE: 20031113

NCL US 6528097 B1 20030304  
 000/424.422; 000/424.501; 000/514.570

#### CTCS CITATION COUNTERS

PNC.DI	0	Cited Patents Count (by inventor)
PNC.DX	48	Cited Patents Count (by examiner)
IAC.DI	0	Cited Issuing Authority Count (by inventor)
IAC.DX	2	Cited Issuing Authority Count (by examiner)
PNC.GI	0	Citing Patents Count (by inventor)
PNC.GX	0	Citing Patents Count (by examiner)
IAC.GI	0	Citing Issuing Authority Count (by inventor)
IAC.GX	0	Citing Issuing Authority Count (by examiner)
CRC.I	0	Cited Literature References Count (by inventor)
CRC.X	20	Cited Literature References Count (by examiner)

CDP CITED PATENTS UPD: 20031113

Cited by Examiner

```

-----
CITING PATENT    CAT    CITED PATENT    ACCNO
-----
US 6528097      B1      EP 52510        A 1982-44213E/22
PA: (SYNT) SYNTEX USA INC
IN: KENT, J S; LEWIS, D H; SANDERS, L M; TICE, T R
    US 3540444    A 1970-84133R/45
PA: (SCHB) SCHERER CORP R P
    US 3773919    A 1971-32146S/19
PA: (DUPO) DU PONT DE NEMOURS & CO E I
    US 3788315    A 1974-10999V/06
PA: (LAUR-I) LAURENS S
    US 4166800    A 1979-68042B/37
PA: (SANO) SANDOZ INC
IN: FONG, F W
    US 4384975    A 1981-95485D/52
PA: (SANO) SANDOZ LTD
IN: FONG, J W
    US 4530840    A 1984-064255/11
PA: (STOL-N) STOLLE RES & DEV; (SOUR) SOUTHERN RES INST
IN: BECK, L R; COWSAR, D R; LEWIS, D H; TICE, T R
    US 4542025    A 1985-248956/40
PA: (SOUR) SOUTHERN RES INST; (STOL-N) STOLLE RES & DEV
IN: BECK, L R; COWSAR, D R; LEWIS, D H; TICE, T R
    US 4585482    A 1986-131060/20
PA: (SOUR) SOUTHERN RES INST
IN: GILLEY, R M; MEYERS, W E; SHANNON, W M; TICE, T R
    US 4622244    A 1986-318526/48
PA: (UNIW) UNIV WASHINGTON
IN: LAPKA, G G; MASON, N S; THIES, C
    US 4637905    A 1987-042802/06
PA: (BATT) BATTELLE DEV CORP
IN: GARDNER, D L
    US 4675189    A 1987-192071/27
PA: (SYNT) SYNTEX (USA)
IN: KENT, J S; LEWIS, D H; RICE, T R; SANDERS, L M
    US 4798786    A 1989-046157/06
PA: (STOL-N) STOLLE RES & DEV
IN: MEYERS, W E; TICE, T R
    US 4835139    A 1987-228660/33
PA: (DEBI-N) DEBIOPHARM SA
IN: MAUVERNAY, R Y; ORSOLINI, P; SCHALLY, A V; TICE, T R
    US 4863735    A 1988-105413/15
PA: (MASI) MASSACHUSETTS INST TECHNOLOGY
IN: FOX, J G; KOHN, J B; LANGER, R S; NIEMI, S M
    US 4897268    A 1989-040741/06
PA: (SOUR) SOUTHERN RES INST
IN: GILLEY, R M; TICE, T R
    US 4938763    A 1990-147718/19
PA: (ATRI-N) ATRIX LAB INC; (SOUR) SOUTHERN RES INST;
    (DUNN-I) DUNN R L
IN: COWSAR, D R; DUNN, R L; ENGLISH, J P; VANDERBILT, D P;
    VANDERBILT, D D
    US 4941880    A 1990-245877/32
PA: (BIOJ-N) BIOJECT INC
IN: BURNS, M
    US 5000886    A 1988-339310/48
PA: (AMCY) AMERICAN CYANAMID CO
IN: LANZILOTTI, M G; LAWTER, J R
    US 5019096    A 1989-235738/33
PA: (UYCO) UNIV COLUMBIA NEW YORK; (UYCO-N) COLUMBIA UNIV
IN: FOX, C L; MODAK, S M; SAMPATH, L A

```



US 5059187 A 1991-332380/45  
PA: (DEYL-N) DEY LABS INC;  
IN: RAFF, A M; SPERRY, C R  
US 5064413 A 1991-141962/20  
PA: (BIOJ-N) BIOJECT INC  
IN: MCKINNON, C N; NAKAGAWA, T; WILCOX, C E  
US 5075109 A 1989-272277/38  
PA: (SOUR) SOUTHERN RES INST; (UABR-N) UAB RES FOUND;  
(UABR-N) UAB RES FOUNDATION  
IN: ELDRIDGE, J H; GILLEY, R M; STAAS, J K; TICE, T R;  
STASS, J K; TICE, T T  
US 5102872 A 1992-141144/17  
PA: (CETU) CETUS CORP  
IN: GILLEY, R M; HUDSON, M E; NUNBERG, J H; SINGH, M;  
TAFORO, T A; TICE, T R  
US 5129825 A 1992-258764/31  
PA: (DISC-I) DISCKO J J; (DISC-I) DISCKO J  
IN: DISCKO, J J; DISCKO, J  
US 5133701 A 1990-376340/51  
PA: (HANS-I) HAN S I  
IN: HAN, S I  
US 5236355 A 1990-211295/28  
PA: (AMCY) AMERICAN CYANAMID CO  
IN: BRIZZOLARA, N S; LANZILOTTI, M G; LAWTER, J R  
US 5278202 A 1990-147718/19  
PA: (ATRI-N) ATRIX LAB INC; (SOUR) SOUTHERN RES INST;  
(DUNN-I) DUNN R L  
IN: COWSAR, D R; DUNN, R L; ENGLISH, J P; VANDERBILT, D P;  
VANDERBILT, D D  
US 5290494 A 1994-074278/09  
PA: (TEXA) UNIV TEXAS SYSTEM  
IN: BOYAN, B D; COOMBES, A G A; HECKMAN, J D  
US 5360610 A 1991-369011/50  
PA: (SOUR) SOUTHERN RES INST  
IN: DILLON, D L; MASON, D W; TICE, T R; DAHLSTROM, A B;  
MCRAE-MCFARLANE, A  
US 5384133 A 1988-063906/09  
PA: (INNO-N) INNOVATA BIOMED LTD; (BOYE-I) BOYES R N  
IN: BOYES, R N; GILLEY, R M; PLEDGER, K L; TICE, T R  
US 5407609 A 1990-361292/48  
PA: (SOUR) SOUTHERN RES INST;  
IN: GILLEY, R M; TICE, T R  
US 5417986 A 1995-199683/26  
PA: (USSA) US SEC OF ARMY  
IN: BOEDEKER, E C; REID, R H; SETTERSTROM, J A; VAN  
HAMONT, J E  
US 5429822 A 1993-303139/38  
PA: (CAMB-N) CAMBRIDGE SCI INC  
IN: AUGENSTEIN, D C; GRESSER, J D; JIMOH, A G; KUETHE, D  
O; TRANTOLO, D J; WISE, D L  
US 5500228 A 1990-211296/28  
PA: (AMCY) AMERICAN CYANAMID CO  
IN: LANZILOTTI, M G; LAWTER, J R  
US 5538739 A 1996-353786/35  
PA: (NOVS) NOVARTIS INC; (SANO) SANDOZ LTD  
IN: BODMER, D; FONG, J W; KISSEL, T; MAULDING, H V;  
NAGELE, O; PEARSON, J E  
US 5639480 A 1997-332008/30  
PA: (NOVS) NOVARTIS INC; (SANO) SANDOZ LTD; (NOVS)  
NOVARTIS AG  
IN: BODMER, D; FONG, J W; KISSEL, T; MAULDING, H V;  
NAGELE, O; PEARSON, J E  
US 5643605 A 1995-170022/22



PA: (GETH) GENENTECH INC  
IN: CLELAND, J L; LIM, A; POWELL, M F  
US 5648096 A 1994-167187/20  
PA: (SCHW-N) SCHWARZ PHARMA AG  
IN: GANDER, B; MERKLE, H P  
US 5650173 A 1995-200182/26  
PA: (ALKE-N) ALKERMES CONTROLLED THERAPEUTICS; (MEDI-N)  
MEDISORB TECHNOLOGIES INT LP  
IN: ATKINS, T J; HAZRATI, A M; HERBERT, P F; RAMSTACK, J  
M; STROBEL, J; RAMSTACK, M J  
US 5688530 A 1992-042911/06  
PA: (SANO) SANDOZ-ERFINDUNGEN VERW GMBH; (SANO) SANDOZ  
LTD; (SANO) SANDOZ AG; (PRIK-I) PRIKOSZOVICH W; (NOVS)  
NOVARTIS AG; (SANO) SANDOZ SA  
IN: PRIKOSZOVICH, W; PRIKOSZOVI, W; BODMER, D; FONG, J W;  
KISSEL, T; MAULDING, H V; NAGELE, O; PEARSON, J E  
US 5693343 A 1998-031704/03  
PA: (USSA) US SEC OF ARMY  
IN: BOEDEKER, E C; BROWN, W R; REID, R H; THIES, C; VAN  
HAMONT, J E  
US 5762965 A 1998-347245/30  
PA: (USSA) US SEC OF ARMY  
IN: BIRX, D L; BURNETT, P R; REID, R H; SETTERSTROM, J A;  
VAN COTT, T C; VAN HAMONT, J E  
US 5811128 A 1998-530832/45  
PA: (SOUR) SOUTHERN RES INST; (UABR-N) UAB RES FOUND  
IN: ELDRIDGE, J H; GILLEY, R M; STAAS, J K; TICE, T R  
US 5814344 A 1998-541706/46  
PA: (SOUR) SOUTHERN RES INST; (UABR-N) UAB RES FOUND  
IN: ELDRIDGE, J H; GILLEY, R M; STAAS, J K; TICE, T R  
US 5820883 A 1998-567595/48  
PA: (SOUR) SOUTHERN RES INST; (UABR-N) UAB RES FOUND  
IN: ELDRIDGE, J H; GILLEY, R M; STAAS, J K; TICE, T R  
US 5853763 A 1999-094826/08  
PA: (SOUR) SOUTHERN RES INST; (UABR-N) UAB RES FOUND  
IN: ELDRIDGE, J H; GILLEY, R M; STAAS, J K; TICE, T R  
US 6217911 2001-396353/42  
PA: (USSA) US SEC OF ARMY  
IN: SETTERSTROM, J A; VAN HAMONT, J E; VAUGN, W M

REN LITERATURE CITATIONS UPR: 20031113

## Citations by Examiner

CITING PATENT CAT CITED LITERATURE

US 6528097	B1	Gilding, Biodegradable polymers for use in surgery-polyglycolic/poly (ac c acid) homo-and copolymers: 1, Polymer, vol. 20, Dec. 1979, ppl459-1464.
US 6528097	B1	Biotechnology News, Aug. 22, 1997, vol. 17, No. 20, Topical DNA vaccine elicits immune response.
US 6528097	B1	Hall, et al., Purification and Analysis of Colonization Factor Antigen I, Coli Surface Antigen I, and Coli Surface ANTigen 3 Fimbriae from Enterotoxigenic Escherichia Coli, Journal of Bacteriology, Nov. 1989, p6372-6374, vol. 171, No. 11.
US 6528097	B1	Evans, et al. Purification and Characterization of the CFR/I Antigen of Enterotoxigenic Escherichia coli, Infection and Immunity, Aug. 1979, p

- 738-748, vol. 25.
- US 6528097 B1 Karjalainen, et al., Molecular Cloning and Nucleotide Sequence of the Colonization Factor Antigen I Gene of *Escherichia coli*, Infection and Immunity, Apr. 1989, p1126-1130, vol. 57.
- US 6528097 B1 Jeyanthi, et al., Novel, Burst Free Programmable Biodegradable Microspheres For Controlled Release of Polypeptides, Proceedings Int. Symp. control Release Bioact. Mater. (1996) p351-352.
- US 6528097 B1 Yeh, A novel emulsification-solvent extraction technique for production of protein loaded biodegradable microparticles for vaccine and drug delivery, Journal of Controlled Release, 33 (1995) 437-445.
- US 6528097 B1 Yan, Characterization and morphological analysis of protein-loaded poly(lactide-co-glycolide) microparticles prepared by water-in-oil-in-water emulsion technique, Journal of Controlled Release, 32 (1994) 231-241.
- US 6528097 B1 Wang, et al., Influence of formulation methods on the in vitro controlled release of protein from poly (ester) microspheres Journal of Controlled Release, 17 (1991) 23-32.
- US 6528097 B1 Brown, Wonder Drugs' Losing Healing Aura, The Washing Post, Jun. 26, 1995, A section.
- US 6528097 B1 Setterstrom, Controlled Release of Antibiotics From biodegradable Microcapsules For Wound infection Control, Chemical Abstracts, 1983, pp215-226.
- US 6528097 B1 Perez-Casal, et al., Gene Encoding the Major Subunit of CS1 Pili of Human Enterotoxigenic *Escherichia Coli*, Infection and Immunity, Nov., 1990, p 3594-3600, vol. 58, No. 11.
- US 6528097 B1 Jordi, et al., Analysis of the first two genes of the CS1 fimbrial operon in human enterotoxigenic *Escherichia coli* of serotype O139: H28, FEMS Microbiology Letters 80, (1991) p265-270.
- US 6528097 B1 Tan, et al., Mapping the Antigenic Epitopes of Human Dihydrofolate Reductase by Systematic Synthesis of Peptides on solid Supports, The Journal of Biological Chemistry, vol. 265, No. 14, Issue of May 15, pp. 8022-8026 (1990).
- US 6528097 B1 McConnel, et al., Antigenic homology within human enterotoxigenic *Escherichia coli* fimbrial colonization factor antigens: CFA/I, coli-surface-associated antigens (CS)1, CS2, CS4 and CS17, FEMS Microbiology Letters 61 (1989) 105-108.
- US 6528097 B1 Van der Zee, Efficient mapping and characterization of a T cell epitope by the simultaneous synthesis of multiple peptides, Eur. J. Immunol. 1989, 19: 43-47.
- US 6528097 B1 Cassels, et al., Analysis of *Escherichia coli* Colonization Factor Antigen I Linear B-Cell Epitopes, as Determined by Primate Responses, following Protein Sequence Verification, Infection and Immunity, Jun. 1992, p. 2174-2181, vol. 60, No. 6.
- US 6528097 B1 Maister, First Oral AIDS Vaccine Trials Near, BioWorld Today, Tuesday, Apr. 19, 1994, p. 4.
- US 6528097 B1 Rognan, et al., Molecular Modeling of an Antigenic Complex Between a Viral Peptide and a Class I Major Histocompatibility Glycoprotein, Proteins

US 6528097 B1

Structure, Function and Genetics 13 70-85 (1992).  
Brown, A hypothetical model of the foreign antigen  
binding site of Class II histocompatibility  
molecules, Nature, vol. 332, Apr. 28, 1988,  
p845-850.

L142 ANSWER 2 OF 6 DPCI COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2003-101718 [09] DPCI

CR 1991-295351 [40]; 1995-199683 [26]; 1996-019737 [02]; 1997-393337 [36];

1998-031704 [03]; 1998-129287 [12]; 1998-347245 [30]; 1998-437043 [37];

2001-396353 [42]; 2003-615263 [58]; 2003-730422 [69]

DNN N2003-081184 DNC C2003-025499

TI Controlled release microcapsule pharmaceutical composition useful in  
treatment of cancer comprises hydrophobic bioactive agent, blend of end  
capped and uncapped biocompatible, biodegradable poly(lactide/glycolide)  
copolymer.

DC A96 B05 B07 D22 P32

IN DUONG, H; JACOB, E; SETTERSTROM, J A; VAN HAMONT, J; VAUGHAN, W; VOOK, N C

PA (USSA) US SEC OF ARMY

CYC 1

PI US 6447796 B1 20020910 (200309)\* 40p A61F013-00

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19950522, CIP of US 1995-446149 19950522, CIP of US 1996-590973

19960124, CIP of US 1996-675895 19960705, CIP of US 1996-698896 19960816,

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of US 6309669

PRAI US 1997-920326 19970821; US 1994-242960 19940516; US 1995-446148

19950522; US 1995-446149 19950522; US 1996-590973 19960124; US

1996-675895 19960705; US 1996-698896 19960816; US 1997-789734

19970127

IC ICM A61F013-00

ICS A61F002-00; A61K009-22; A61K009-32

FS CPI GMPI

EXF. EXAMINER'S FIELD OF SEARCH UPE: 20030604

NCL US 6447796 B1 20020910

000/424.422; 000/424.426; 000/424.457; 000/424.468

## CTCS CITATION COUNTERS

PNC.DI	0	Cited Patents Count (by inventor)
PNC.DX	47	Cited Patents Count (by examiner)
IAC.DI	0	Cited Issuing Authority Count (by inventor)
IAC.DX	2	Cited Issuing Authority Count (by examiner)

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CDP CITED PATENTS UPD: 20030604

Cited by Examiner

CITING PATENT CAT CITED PATENT ACCNO

-----  
 US 6447796 B1 EP 52510 A 1982-44213E/22  
 PA: (SYNT) SYNTEX USA INC  
 IN: KENT, J S; LEWIS, D H; SANDERS, L M; TICE, T R  
 US 3540444 A 1970-84133R/45  
 PA: (SCHB) SCHERER CORP R P  
 US 3773919 A 1971-32146S/19  
 PA: (DUPO) DU PONT DE NEMOURS & CO E I  
 US 3788315 A 1974-10999V/06  
 PA: (LAUR-I) LAURENS S  
 US 4166800 A 1979-68042B/37  
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 US 4384975 A 1981-95485D/52  
 PA: (SANO) SANDOZ LTD  
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 US 4530840 A 1984-064255/11  
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 US 4542025 A 1985-248956/40  
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 US 4585482 A 1986-131060/20  
 PA: (SOUR) SOUTHERN RES INST  
 IN: GILLEY, R M; MEYERS, W E; SHANNON, W M; TICE, T R  
 US 4622244 A 1986-318526/48  
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 US 4637905 A 1987-042802/06  
 PA: (BATT) BATTELLE DEV CORP  
 IN: GARDNER, D L  
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 IN: KENT, J S; LEWIS, D H; RICE, T R; SANDERS, L M  
 US 4798786 A 1989-046157/06  
 PA: (STOL-N) STOLLE RES & DEV  
 IN: MEYERS, W E; TICE, T R  
 US 4835139 A 1987-228660/33  
 PA: (DEBI-N) DEBIOPHARM SA  
 IN: MAUVERNAY, R Y; ORSOLINI, P; SCHALLY, A V; TICE, T R  
 US 4863735 A 1988-105413/15  
 PA: (MASI) MASSACHUSETTS INST TECHNOLOGY  
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 US 4897268 A 1989-040741/06  
 PA: (SOUR) SOUTHERN RES INST  
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 US 4938763 A 1990-147718/19  
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 VANDERBILT, D D  
 US 4941880 A 1990-245877/32  
 PA: (BIOJ-N) BIOJECT INC  
 IN: BURNS, M  
 US 5000886 A 1988-339310/48  
 PA: (AMCY) AMERICAN CYANAMID CO  
 IN: LANZILOTTI, M G; LAWTER, J R  
 US 5019096 A 1989-235738/33  
 PA: (UYCO) UNIV COLUMBIA NEW YORK; (UYCO-N) COLUMBIA UNIV  
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 US 5059187 A 1991-332380/45  
 PA: (DEYL-N) DEY LABS INC;  
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US 5064413 A 1991-141962/20  
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US 5102872 A 1992-141144/17  
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TAFORO, T A; TICE, T R  
US 5129825 A 1992-258764/31  
PA: (DISC-I) DISCKO J J; (DISC-I) DISCKO J  
IN: DISCKO, J J; DISCKO, J  
US 5133701 A 1990-376340/51  
PA: (HANS-I) HAN S I  
IN: HAN, S I  
US 5236355 A 1990-211295/28  
PA: (AMCY) AMERICAN CYANAMID CO  
IN: BRIZZOLARA, N S; LANZILOTTI, M G; LAWTER, J R  
US 5278202 A 1990-147718/19  
PA: (ATRI-N) ATRIX LAB INC; (SOUR) SOUTHERN RES INST;  
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US 5290494 A 1994-074278/09  
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US 5360610 A 1991-369011/50  
PA: (SOUR) SOUTHERN RES INST  
IN: DILLON, D L; MASON, D W; TICE, T R; DAHLSTROM, A B;  
MCRAE-MCFARLANE, A  
US 5384133 A 1988-063906/09  
PA: (INNO-N) INNOVATA BIOMED LTD; (BOYE-I) BOYES R N  
IN: BOYES, R N; GILLEY, R M; PLEDGER, K L; TICE, T R  
US 5407609 A 1990-361292/48  
PA: (SOUR) SOUTHERN RES INST;  
IN: GILLEY, R M; TICE, T R  
US 5417986 A 1995-199683/26  
PA: (USSA) US SEC OF ARMY  
IN: BOEDEKER, E C; REID, R H; SETTERSTROM, J A; VAN  
HAMONT, J E  
US 5429822 A 1993-303139/38  
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IN: AUGENSTEIN, D C; GRESSER, J D; JIMOH, A G; KUETHE, D  
O; TRANTOLO, D J; WISE, D L  
US 5500228 A 1990-211296/28  
PA: (AMCY) AMERICAN CYANAMID CO  
IN: LANZILOTTI, M G; LAWTER, J R  
US 5538739 A 1996-353786/35  
PA: (NOVS) NOVARTIS INC; (SANO) SANDOZ LTD  
IN: BODMER, D; FONG, J W; KISSEL, T; MAULDING, H V;  
NAGELE, O; PEARSON, J E  
US 5639480 A 1997-332008/30  
PA: (NOVS) NOVARTIS INC; (SANO) SANDOZ LTD; (NOVS)  
NOVARTIS AG  
IN: BODMER, D; FONG, J W; KISSEL, T; MAULDING, H V;  
NAGELE, O; PEARSON, J E  
US 5643605 A 1995-170022/22  
PA: (GETH) GENENTECH INC  
IN: CLELAND, J L; LIM, A; POWELL, M F  
US 5648096 A 1994-167187/20

PA: (SCHW-N) SCHWARZ PHARMA AG  
 IN: GANDER, B; MERKLE, H P  
 US 5650173 A 1995-200182/26

PA: (ALKE-N) ALKERMES CONTROLLED THERAPEUTICS; (MEDI-N) MEDISORB TECHNOLOGIES INT LP  
 IN: ATKINS, T J; HAZRATI, A M; HERBERT, P F; RAMSTACK, J M; STROBEL, J; RAMSTACK, M J  
 US 5688530 A 1992-042911/06

PA: (SANO) SANDOZ-ERFINDUNGEN VERW GMBH; (SANO) SANDOZ LTD; (SANO) SANDOZ AG; (PRIK-I) PRIKOSZOVICH W; (NOVS) NOVARTIS AG; (SANO) SANDOZ SA  
 IN: PRIKOSZOVICH, W; PRIKOSZOVI, W; BODMER, D; FONG, J W; KISSEL, T; MAULDING, H V; NAGELE, O; PEARSON, J E  
 US 5693343 A 1998-031704/03

PA: (USSA) US SEC OF ARMY  
 IN: BOEDEKER, E C; BROWN, W R; REID, R H; THIES, C; VAN HAMONT, J E  
 US 5762965 A 1998-347245/30

PA: (USSA) US SEC OF ARMY  
 IN: BIRX, D L; BURNETT, P R; REID, R H; SETTERSTROM, J A; VAN COTT, T C; VAN HAMONT, J E  
 US 5811128 A 1998-530832/45

PA: (SOUR) SOUTHERN RES INST; (UABR-N) UAB RES FOUND  
 IN: ELDRIDGE, J H; GILLEY, R M; STAAS, J K; TICE, T R  
 US 5814344 A 1998-541706/46

PA: (SOUR) SOUTHERN RES INST; (UABR-N) UAB RES FOUND  
 IN: ELDRIDGE, J H; GILLEY, R M; STAAS, J K; TICE, T R  
 US 5820883 A 1998-567595/48

PA: (SOUR) SOUTHERN RES INST; (UABR-N) UAB RES FOUND  
 IN: ELDRIDGE, J H; GILLEY, R M; STAAS, J K; TICE, T R  
 US 5853763 A 1999-094826/08

PA: (SOUR) SOUTHERN RES INST; (UABR-N) UAB RES FOUND  
 IN: ELDRIDGE, J H; GILLEY, R M; STAAS, J K; TICE, T R

## REN LITERATURE CITATIONS UPR: 20030604

## Citations by Examiner

CITING PATENT	CAT	CITED LITERATURE
US 6447796	B1	Gilding, Biodegradable polymers for use in surgery-polyglycolic/poly (ac c acid)homo- and copolymers: 1, Polymer, vol. 20, Dec. 1979, pp. 1459-1464.
US 6447796	B1	Biotechnology News, Aug. 22, 1997, vol. 17, No. 20, Topical DNA vaccine elicits immune response.
US 6447796	B1	Hall, et al., Purification and Analysis of Colonization Factor Antigen I, Coli Surface Antigen 1, and Coli Surface Antigen 3 Fimbriae from Enterotoxigenic Escherichia Coli, Journal of Bacteriology, Nov. 1989, pp. 6372-6374, vol. 171, No. 11.
US 6447796	B1	Evans, et al. Purification and Characterization of the CFR/I Antigen of Enterotoxigenic Escherichia coli, Infection and Immunity, Aug. 1979, pp. 738-748, vol. 25.
US 6447796	B1	Karjalainen, et al., Molecular Cloning and Nucleotide Sequence of the Colonization Factor Antigen I Gene of Escherichia coli, Infection and Immunity, Apr. 1989, pp. 1126-1130, vol. 57.
US 6447796	B1	Jeyanthi, et al., Novel, Burst Free Programmable



- Biodegradable Microspheres For Controlled Release of Polypeptides, Proceedings Int. Symp. control Release Bioact. Mater. (1996) pp. 351-352.
- US 6447796 B1 Yeh, A novel emulsification-solvent extraction technique for production of protein loaded biodegradable microparticles for vaccine and drug delivery, Journal of Controlled Release, 33 (10,0,5) 437-445.
- US 6447796 B1 Yan, Characterization and morphological analysis of protein-loaded poly(lactide-co-glycolide) microparticles prepared by water-in-oil-in-water emulsion technique, Journal of Controlled Release, 32 (1994) 231-241.
- US 6447796 B1 Wang, et al., Influence of formulation methods on the in vitro controlled release of protein from poly(ester) microspheres Journal of Controlled Release, 17 (1991) 23-32.
- US 6447796 B1 Brown, Wonder Drugs' Losing Healing Aura, The Washing Post, Jun. 26, 1995, A section.
- US 6447796 B1 Setterstrom, Controlled Release of Antibiotics From biodegradable Microcapsules For Wound infection Control, Chemical Abstracts, 1983, pp. 215-226.
- US 6447796 B1 Perez-Casal, et al., Gene Encoding the Major Subunit of CS1 Pili of Human Enterotoxigenic Escherichia Coli, Infection and Immunity, Nov., 1990, pp. 3594-3600, vol. 58, No. 11.
- US 6447796 B1 Jordi, et al., Analysis of the first two genes of the CS1 fimbrial operon in human enterotoxigenic Escherichia coli of serotype O139: H20, FEMS Microbiology Letters 80, (1991) pp. 265-270.
- US 6447796 B1 Tan, et al., Mapping the Antigenic Epitopes of Human Dihydrofolate Reductase by Systematic Synthesis of Peptides on solid Supports, The Journal of Biological Chemistry, vol. 265, No. 14, Issue of May 15, pp. 8022-8026 (1990).
- US 6447796 B1 McConnel, et al., Antigenic homology within human enterotoxigenic Escherichia coli fimbrial colonization factor antigens: CFA/I, coli-surface-associated antigens (CS)1, CS2, CS4 and CS17, FEMS Microbiology Letters 61 (1989) 105-108.
- US 6447796 B1 Van der Zee, Efficient mapping and characterization of a T cell epitope by the simultaneous synthesis of multiple peptides, Eur. J. Immunol. 1989, 19: 43-47.
- US 6447796 B1 Cassels, et al., Analysis of Escherichia coli Colonization Factor Antigen I Linear B-Cell Epitopes, as Determined by Primate Responses, following Protein Sequence Verification, Infection and Immunity, Jun. 1992, pp. 2174-2181, vol. 60, No. 6.
- US 6447796 B1 Romagnoli, et al. Peptide-MHC Interaction: A Rational Approach to Vaccine Design, Inter. RE. Immunol. 6, 1990, 00 61-73.
- US 6447796 B1 Maister, First Oral AIDS Vaccine Trials Near, BioWorld Today, Tuesday, Apr. 19, 1994, p. 4.
- US 6447796 B1 Rognan, et al., Molecular Modeling of an Antigenic Complex Between a Viral Peptide and a Class I Major Histocompatibility Glycoprotein, Proteins Structure, Function and Genetics 13 70-85 (1992).
- US 6447796 B1 Brown, A hypothetical model of the foreign antigen binding site of Class II histocompatibility

molecules, Nature, vol. 332, Apr. 28, 1988, pp. 845-850.

L142 ANSWER 3 OF 6 DPCI COPYRIGHT 2004 THOMSON DERWENT on STN  
 AN 2001-396353 [42] DPCI  
 CR 1991-295351 [40]; 1995-199683 [26]; 1996-019737 [02]; 1997-393337 [36];  
 1998-031704 [03]; 1998-129287 [12]; 1998-347245 [30]; 1998-437043 [37];  
 2003-101718 [09]; 2003-615263 [58]; 2003-730422 [69]  
 DNC C2001-I20531  
 TI Microcapsule formulation for controlled release of a nonsteroidal  
 antiinflammatory drug includes a mixture of capped and uncapped  
 biocompatible biodegradable lactide/glycolide copolymers.  
 DC A96 B05  
 IN SETTERSTROM, J A; VAN HAMONT, J E; VAUGN, W M  
 PA (USSA) US SEC OF ARMY  
 CYC 1  
 PI US 6217911 B1 20010417 (200142)\* 16p A61K009-50  
 ADT US 6217911 B1 CIP of US 1995-446149 19950522, US 1996-675895  
 19960705  
 PRAI US 1996-675895 19960705; US 1995-446149 19950522  
 IC ICM A61K009-50  
 FS CPI

EXF EXAMINER'S FIELD OF SEARCH UPE: 20010807

NCL US 6217911 B1 20010417  
 000/424.422; 000/424.423; 000/424.425; 000/424.426; 000/424.444;  
 000/424.484; 000/424.486; 000/424.489; 000/424.490; 000/424.497;  
 000/424.501; 000/514.570; 000/514.626; 000/514.818; 000/514.887;  
 000/514.944; 000/514.953; 000/514.963; 000/514.965

# CTCS CITATION COUNTERS

PNC.DI	0	Cited Patents Count (by inventor)
PNC.DX	51	Cited Patents Count (by examiner)
IAC.DI	0	Cited Issuing Authority Count (by inventor)
IAC.DX	2	Cited Issuing Authority Count (by examiner)
PNC.GI	0	Citing Patents Count (by inventor)
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IAC.GX	1	Citing Issuing Authority Count (by examiner)
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CRC.X	21	Cited Literature References Count (by examiner)

CDP CITED PATENTS UPD: 20010807

Cited by Examiner

CITING PATENT	CAT	CITED PATENT	ACCNO
US 6217911	B1	EP 52510	B2 1982-44213E/22
	PA:	(SYNT) SYNTEX USA INC	
	IN:	KENT, J S; LEWIS, D H; SANDERS, L M; TICE, T R	
		US 3540444	A 1970-84133R/45
	PA:	(SCHB) SCHERER CORP R P	
		US 3773919	A 1971-32146S/19
	PA:	(DUPO) DU PONT DE NEMOURS & CO E I	
		US 3788315	A 1974-10999V/06

PA: (LAUR-I) LAURENS S  
US 4166800 A 1979-68042B/37  
PA: (SANO) SANDOZ INC  
IN: FONG, F W  
US 4384975 A 1981-95485D/52  
PA: (SANO) SANDOZ LTD  
IN: FONG, J W  
US 4530840 A 1984-064255/11  
PA: (STOL-N) STOLLE RES & DEV; (SOUR) SOUTHERN RES INST  
IN: BECK, L R; COWSAR, D R; LEWIS, D H; TICE, T R  
US 4542025 A 1985-248956/40  
PA: (SOUR) SOUTHERN RES INST; (STOL-N) STOLLE RES & DEV  
IN: BECK, L R; COWSAR, D R; LEWIS, D H; TICE, T R  
US 4585482 A 1986-131060/20  
PA: (SOUR) SOUTHERN RES INST  
IN: GILLEY, R M; MEYERS, W E; SHANNON, W M; TICE, T R  
US 4622244 A 1986-318526/48  
PA: (UNIW) UNIV WASHINGTON  
IN: LAPKA, G G; MASON, N S; THIES, C  
US 4637905 A 1987-042802/06  
PA: (BATT) BATTELLE DEV CORP  
IN: GARDNER, D L  
US 4675189 A 1987-192071/27  
PA: (SYNT) SYNTEX (USA)  
IN: KENT, J S; LEWIS, D H; RICE, T R; SANDERS, L M  
US 4798786 A 1989-046157/06  
PA: (STOL-N) STOLLE RES & DEV  
IN: MEYERS, W E; TICE, T R  
US 4835139 A 1987-228660/33  
PA: (DEBI-N) DEBIOPHARM SA  
IN: MAUVERNAY, R Y; ORSOLINI, P; SCHALLY, A V; TICE, T R  
US 4863735 A 1988-105413/15  
PA: (MASS) MASSACHUSETTS INST TECHNOLOGY  
IN: FOX, J G; KOHN, J B; LANGER, R S; NIEMI, S M  
US 4897268 A 1989-040741/06  
PA: (SOUR) SOUTHERN RES INST  
IN: GILLEY, R M; TICE, T R  
US 4937254 A 1990-216851/28  
PA: (ETHI) ETHICON INC  
IN: DIZEREGA, G S; JOHNS, D B; RICHER, L R; SHALABY, S W;  
SHEFFIELD, W D; LEROY, L R  
US 4938763 A 1990-147718/19  
PA: (ATRI-N) ATRIX LAB INC; (DUNN-I) DUNN R L; (SOUR)  
SOUTHERN RES INST  
IN: COWSAR, D R; DUNN, R L; ENGLISH, J P; VANDERBILT, D P;  
VANDERBILT, D D  
US 4941880 A 1990-245877/32  
PA: (BIOJ-N) BIOJECT INC  
IN: BURNS, M  
US 5000886 A 1988-339310/48  
PA: (AMCY) AMERICAN CYANAMID CO  
IN: LANZILOTTI, M G; LAWTER, J R  
US 5019096 A 1989-235738/33  
PA: (UYCO) UNIV COLUMBIA NEW YORK; (UYCO-N) COLUMBIA UNIV  
IN: FOX, C L; MODAK, S M; SAMPATH, L A  
US 5059187 A 1991-332380/45  
PA: (DEYL-N) DEY LABS INC;  
IN: RAFF, A M; SPERRY, C R  
US 5064413 A 1991-141962/20  
PA: (BIOJ-N) BIOJECT INC  
IN: MCKINNON, C N; NAKAGAWA, T; WILCOX, C E  
US 5075109 A 1989-272277/38  
PA: (SOUR) SOUTHERN RES INST; (UABR-N) UAB RES FOUND;

(UABR-N) UAB RES FOUNDATION  
IN: ELDRIDGE, J H; GILLEY, R M; STAAS, J K; TICE, T R;  
STASS, J K; TICE, T T  
US 5102872 A 1992-141144/17  
PA: (CETU) CETUS CORP  
IN: GILLEY, R M; HUDSON, M E; NUNBERG, J H; SINGH, M;  
TAFORO, T A; TICE, T R  
US 5129825 A 1992-258764/31  
PA: (DISC-I) DISCKO J J; (DISC-I) DISCKO J  
IN: DISCKO, J J; DISCKO, J  
US 5133701 A 1990-376340/51  
PA: (HANS-I) HAN S I  
IN: HAN, S I  
US 5236355 A 1990-211295/28  
PA: (AMCY) AMERICAN CYANAMID CO  
IN: BRIZZOLARA, N S; LANZILOTTI, M G; LAWTER, J R  
US 5278202 A 1990-147718/19  
PA: (ATRI-N) ATRIX LAB INC; (DUNN-I) DUNN R L; (SOUR)  
SOUTHERN RES INST  
IN: COWSAR, D R; DUNN, R L; ENGLISH, J P; VANDERBILT, D P;  
VANDERBILT, D D  
US 5290494 A 1994-074278/09  
PA: (TEXA) UNIV TEXAS SYSTEM  
IN: BOYAN, B D; COOMBES, A G A; HECKMAN, J D  
US 5360610 A 1991-369011/50  
PA: (SOUR) SOUTHERN RES INST  
IN: DILLON, D L; MASON, D W; TICE, T R; DAHLSTROM, A B;  
MCRAE-MCFARLANE, A  
US 5384133 A 1988-063906/09  
PA: (INNO-N) INNOVATA BIOMED LTD; (BOYE-I) BOYES R N  
IN: BOYES, R N; GILLEY, R M; PLEDGER, K L; TICE, T R  
US 5407609 A 1990-361292/48  
PA: (SOUR) SOUTHERN RES INST;  
IN: GILLEY, R M; TICE, T R  
US 5417986 A 1995-199683/26  
PA: (USSA) US SEC OF ARMY  
IN: BOEDEKER, E C; REID, R H; SETTERSTROM, J A; VAN  
HAMONT, J E  
US 5429822 A 1993-303139/38  
PA: (CAMB-N) CAMBRIDGE SCI INC  
IN: AUGENSTEIN, D C; GRESSER, J D; JIMOH, A G; KUETHE, D  
O; TRANLOLO, D J; WISE, D L  
US 5500228 A 1990-211296/28  
PA: (AMCY) AMERICAN CYANAMID CO  
IN: LANZILOTTI, M G; LAWTER, J R  
US 5538739 A 1996-353786/35  
PA: (SANO) SANDOZ LTD  
IN: BODMER, D; FONG, J W; KISSEL, T; MAULDING, H V;  
NAGELE, O; PEARSON, J E  
US 5612052 A 1996-457292/46  
PA: (POLY-N) POLY-MED INC;  
IN: SHALABY, S W  
US 5622998 A 1996-152662/16  
PA: (KAOS) KAO CORP; (NITL) NITTO DENKO CORP; (SUMR)  
SUMITOMO RUBBER IND LTD; (FUJI-N) FUJI LATEX KK  
IN: HAYASHI, M; KANAMARU, E; KAWASAKI, A; SAKAKI, T;  
SHIBATA, K; TANAKA, Y  
US 5639480 A 1997-332008/30  
PA: (SANO) SANDOZ LTD; (NOVS) NOVARTIS AG  
IN: BODMER, D; FONG, J W; KISSEL, T; MAULDING, H V;  
NAGELE, O; PEARSON, J E  
US 5643605 A 1995-170022/22  
PA: (GETH) GENENTECH INC

IN: CLELAND, J L; LIM, A; POWELL, M F  
 US 5648096 A 1994-167187/20  
 PA: (SCHW-N) SCHWARZ PHARMA AG  
 IN: GANDER, B; MERKLE, H P  
 US 5650173 A 1995-200182/26  
 PA: (ALKE-N) ALKERMES CONTROLLED THERAPEUTICS; (MEDI-N)  
 MEDISORB TECHNOLOGIES INT LP  
 IN: ATKINS, T J; HAZRATI, A M; HERBERT, P F; RAMSTACK, J  
 M; STROBEL, J; RAMSTACK, M J  
 US 5688530 A 1992-042911/06  
 PA: (SANO) SANDOZ-ERFINDUNGEN VERW GMBH; (SANO) SANDOZ  
 LTD; (SANO) SANDOZ AG; (PRIK-I) PRIKOSZOVICH W; (NOVS)  
 NOVARTIS AG; (SANO) SANDOZ SA  
 IN: PRIKOSZOVICH, W; PRIKOSZOVI, W; BODMER, D; FONG, J W;  
 KISSEL, T; MAULDING, H V; NAGELE, O; PEARSON, J E  
 US 5693343 A 1998-031704/03  
 PA: (USSA) US SEC OF ARMY  
 IN: BOEDEKER, E C; BROWN, W R; REID, R H; THIES, C; VAN  
 HAMONT, J E  
 US 5714159 A 1996-457292/46  
 PA: (POLY-N) POLY-MED INC  
 IN: SHALABY, S W  
 US 5762965 A 1998-347245/30  
 PA: (USSA) US SEC OF ARMY  
 IN: BIRX, D L; BURNETT, P R; REID, R H; SETTERSTROM, J A;  
 VAN COTT, T C; VAN HAMONT, J E  
 US 5811128 A 1998-530832/45  
 PA: (SOUR) SOUTHERN RES INST; (UABR-N) UAB RES FOUND  
 IN: ELDRIDGE, J H; GILLEY, R M; STAAS, J K; TICE, T R  
 US 5814344 A 1998-541706/46  
 PA: (SOUR) SOUTHERN RES INST; (UABR-N) UAB RES FOUND  
 IN: ELDRIDGE, J H; GILLEY, R M; STAAS, J K; TICE, T R  
 US 5820883 A 1998-567595/48  
 PA: (SOUR) SOUTHERN RES INST; (UABR-N) UAB RES FOUND  
 IN: ELDRIDGE, J H; GILLEY, R M; STAAS, J K; TICE, T R  
 US 5853763 A 1999-094826/08  
 PA: (SOUR) SOUTHERN RES INST; (UABR-N) UAB RES FOUND  
 IN: ELDRIDGE, J H; GILLEY, R M; STAAS, J K; TICE, T R

REN LITERATURE CITATIONS UPR: 20010807

Citations by Examiner

CITING PATENT CAT CITED LITERATURE

US 6217911	B1	Gilding, Biodegradable polymers for use in surgery-polyglycolic/poly (ac c acid) homo-and copolymers: 1, Polymer, vol. 20, Dec. 1979, pp 1459-1464.
US 6217911	B1	Biotechnology News, Aug. 22, 1997, vol. 17, No. 20, Topical DNA vaccine elicits immune response.
US 6217911	B1	Hall, et al., Purification and Analysis of Colonization Factor Antigen I, Coli Surface Antigen 1, and Coli Surface Antigen 3 Fimbriae from Enterotoxigenic Escherichia Coli, Journal of Bacteriology, Nov. 1989, p 6372-6374, vol. 171, No. 11.
US 6217911	B1	Evans, et al. Purification and Characterization of the CFR/I Antigen of Enterotoxigenic Escherichia coli, Infection and Immunity, Aug. 1979, p 738-748, vol. 25.

- US 6217911 B1 Karjalainen, et al., Molecular Cloning and Nucleotide Sequence of the Colonization Factor Antigen I Gene of *Escherichia coli*, Infection and Immunity, Apr. 1989, p1126-1130, vol. 57.
- US 6217911 B1 Jeyanthi, et al., Novel, Burst Free Programmable Biodegradable Microspheres For Controlled Release of Polypeptides, Proceedings Int. Symp. control Release Bioact. Mater. (1996) p351-352/.
- US 6217911 BI Yeh, A novel emulsification-solvent extraction technique for production of protein loaded biodegradable microparticles for vaccine and drug delivery, Journal of Controlled Release, 33 (1005) 437-445.
- US 6217911 B1 Yan, Characterization and morphological analysis of protein-loaded poly(lactide-co-glycolide) microparticles prepared by water-in-oil-in-water emulsion technique, Journal of Controlled Release, 32 (1994) 231-241.
- US 6217911 B1 Wang, et al., Influence of formulation methods on the in vitro controlled release of protein from poly (ester) microspheres Journal of Controlled Release, 17 (1991) 23-32.
- US 6217911 B1 Brown, Wonder Drugs' Losing Healing Aura, The Washing Post, Jun. 26, 1995, A section.
- US 6217911 B1 Setterstrom, Controlled Release of Antibiotics From biodegradable Microcapsules For Wound infection Control, Chemical Abstracts, 1983, pp215-226.
- US 6217911 B1 Perez-Casal, et al., Gene Encoding the Major Subunit of CS1 Pili of Human Enterotoxigenic *Escherichia coli*, Infection and Immunity, Nov., 1990, p 3594-3600, vol. 58, No. 11.
- US 6217911 B1 Jordi, et al., Analysis of the first two genes of the CS1 fimbrial operon in human enterotoxigenic *Escherichia coli* of serotype O139: H28, FEMS Microbiology Letters 80, (1991) p265-270.
- US 6217911 B1 Tan, et al., Mapping the Antigenic Epitopes of Human Dihydrofolate Reductase by Systematic Synthesis of Peptides on solid Supports, The Journal of Biological Chemistry, vol. 265, No. 14, Issue of May 15, pp. 8022-8026 (1990).
- US 6217911 B1 McConnel, et al., Antigenic homology within human enterotoxigenic *Escherichia coli* fimbrial colonization factor antigens: CFA/I, coli-surface-associated antigens (CS)1, CS2, CS4 and CS17, FEMS Microbiology Letters 61 (1989) 105-108.
- US 6217911 B1 Van der Zee, Efficient mapping and characterization of a T cell epitope by the simultaneous synthesis of multiple peptides, Eur. J. Immunol. 1989, 19: 43-47.
- US 6217911 B1 Cassels, et al., Analysis of *Escherichia coli* Colonization Factor Antigen I Linear B-Cell Epitopes, as Determined by Primate Responses, following Protein Sequence Verification, Infection and Immunity, Jun. 1992, p. 2174-2181, vol. 60, No. 6.
- US 6217911 B1 Romagnoli, et al. Peptide-MHC Interaction: A Rational Approach to Vaccine Design, Inter. RE. Immunol. 6, 1990, 00 61-73.
- US 6217911 B1 Maister, First Oral AIDS Vaccine Trials Near, BioWorld Today, Tuesday, Apr. 19, 1994, p. 4.
- US 6217911 B1 Rognan, et al., Molecular Modeling of an Antigenic

US 6217911 B1 Complex Between a Viral Peptide and a Class I Major Histocompatibility Glycoprotein, Proteins Structure, Function and Genetics 13 70-85 (1992). Brown, A hypothetical model of the foreign antigen binding site of Class II histocompatibility molecules, Nature, vol. 332, Apr. 28, 1988, p845-850.

CGP CITING PATENTS

UPG: 20040115

## Cited by Examiner

CITED PATENT	CAT	CITING PATENT	ACCNO
US 6217911	B1	US 6645521	B2 2001-355172/32
		PA: (EPIC-N) EPICEPT INC; (AMPH-N) AMERICAN PHARMED LABS INC; (EPIC-N) EPICEPT CORP	
		IN: CASSEL, R D; DOUGLAS, C R	

L142 ANSWER 4 OF 6 DPCI COPYRIGHT 2004 THOMSON DERWENT on STN

AN 1998-437043 [37] DPCI

CR 1991-295351 [40]; 1995-199683 [26]; 1996-019737 [02]; 1997-393337 [36]; 1998-031704 [03]; 1998-129287 [12]; 1998-347245 [30]; 2001-396353 [42]; 2003-101718 [09]; 2003-615263 [58]; 2003-730043 [69]; 2003-730422 [69]

DNC C1998-132804

TI New burst-free, sustained, programmable release composition(s) - containing an active material in a blend of uncapped and end-capped co polymer, preferably a poly (DL-lactide-co glycolide).

DC A96 B04 B05 B07 D16 P73

IN BOEDEKER, E C; BROWN, W; CASSELS, F; FRIDEN, P; JACOB, E; JARBOE, D L; JEYANTHI, R; MCQUEEN, C E; REID, R H; ROBERTS, F D; SETTERSTROM, J A; THIES, C; TICE, T R; VAN HAMONT, J E

PA (USSA) US SEC OF ARMY

CYC 79

PI WO 9832427 A1 19980730 (199837)\* EN 422p A61K009-52 <--

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AU 9863175 A 19980818 (199851)

US 6309669 B1 20011030 (200172) A61K009-52

US 6410056 B1 20020625 (200246)# A61K009-50

ADT WO 9832427 A1 WO 1998-US1556 19980127; AU 9863175 A AU 1998-63175 19980127; US 6309669 B1 Cont of US 1984-590308 19840306, CIP of US 1984-590308 19840316, CIP of US 1992-867301 19920410, CIP of US 1995-446148 19950522, CIP of US 1995-446149 19950522, CIP of US 1996-590973 19960124, US 1997-789734 19970127; US 6410056 B1 CIP of US 1984-590308 19840316, CIP of US 1990-493597 19900315, CIP of US 1994-209350 19940107, US 1995-446148 19950522

FDT AU 9863175 A Based on WO 9832427; US 6309669 B1 CIP of US 5417986

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IC ICM A61K009-50; A61K009-52

ICS A61K047-30; B32B005-16

FS CPI GMP1

EXF EXAMINER'S FIELD OF SEARCH UPE: 20030131

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 000/424.486; 000/424.780 .08; 000/424.780 .17; 000/514.200; 000/514.772 .6  
 US 6410056 B1 20020625  
 000/424.457; 000/424.462; 000/424.501; 000/424.502; 000/424.780 .1;  
 000/428.402 .21; 000/514.772 .3; 000/549.274

## CTCS CITATION COUNTERS

PNC.DI	0	Cited Patents Count (by inventor)
PNC.DX	57	Cited Patents Count (by examiner)
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IAC.DX	2	Cited Issuing Authority Count (by examiner)
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PNC.GX	7	Citing Patents Count (by examiner)
IAC.GI	0	Citing Issuing Authority Count (by inventor)
IAC.GX	4	Citing Issuing Authority Count (by examiner)
CRC.I	0	Cited Literature References Count (by inventor)
CRC.X	34	Cited Literature References Count (by examiner)

CDP CITED PATENTS UPD: 20030131

## Cited by Examiner

CITING PATENT	CAT	CITED PATENT	ACCNO
US 6309669	B1	EP 52510	B2 1982-44213E/22
PA:		(SYNT) SYNTEX USA INC	
IN:		KENT, J S; LEWIS, D H; SANDERS, L M; TICE, T R	
		US 4637905	A 1987-042802/06
PA:		(BATT) BATTELLE DEV CORP	
IN:		GARDNER, D L	
		US 4675189	A 1987-192071/27
PA:		(SYNT) SYNTEX (USA)	
IN:		KENT, J S; LEWIS, D H; RICE, T R; SANDERS, L M	
		US 5198220	A 1991-165976/23
PA:		(DAMA-I) DAMANI N C; (PROC) PROCTER & GAMBLE CO	
IN:		DAMANI, N C	
		US 5538739	A 1996-353786/35
PA:		(SANO) SANDOZ LTD	
IN:		BODMER, D; FONG, J W; KISSEL, T; MAULDING, H V;	
		NAGELE, O; PEARSON, J E	
		US 5639480	A 1997-332008/30
PA:		(SANO) SANDOZ LTD; (NOVS) NOVARTIS AG	
IN:		BODMER, D; FONG, J W; KISSEL, T; MAULDING, H V;	
		NAGELE, O; PEARSON, J E	
		US 5643605	A 1995-170022/22
PA:		(GETH) GENENTECH INC	
IN:		CLELAND, J L; LIM, A; POWELL, M F	
		US 5688530	A 1992-042911/06
PA:		(SANO) SANDOZ-ERFINDUNGEN VERW GMBH; (SANO) SANDOZ	
		LTD; (SANO) SANDOZ AG; (PRIK-I) PRIKOSZOVICH W; (NOVS)	
		NOVARTIS AG; (SANO) SANDOZ SA	
IN:		PRIKOSZOVICH, W; PRIKOSZOVI, W; BODMER, D; FONG, J W;	
		KISSEL, T; MAULDING, H V; NAGELE, O; PEARSON, J E	
		US 5707647	A 1995-382728/49
PA:		(ATRI-N) ATRIX LAB INC	
IN:		DUNN, R L; SOUTHLAND, J L; URHEIM, J E; YEWEEY, G L;	



SOUTHARD, J L  
 US 5716981 A 1995-074997/10  
 PA: (ANGI-N) ANGIOGENESIS TECHNOLOGIES INC; (UYBR-N) UNIV  
 BRITISH COLUMBIA; (ANGI-N) ANGIOTECH PHARM INC;  
 (ANGI-N) ANGIOTECH PHAR INC  
 IN: ARSENAULT, A L; BURT, H M; HUNTER, W L; JACKSON, J K;  
 MACHAN, L S; ARSENAULT, L A; ARSENAULT, A  
 US 5886026 A 1995-074997/10  
 PA: (ANGI-N) ANGIOGENESIS TECHNOLOGIES INC; (UYBR-N) UNIV  
 BRITISH COLUMBIA; (ANGI-N) ANGIOTECH PHARM INC;  
 (ANGI-N) ANGIOTECH PHAR INC  
 IN: ARSENAULT, A L; BURT, H M; HUNTER, W L; JACKSON, J K;  
 MACHAN, L S; ARSENAULT, L A; ARSENAULT, A  
 US 5942253 A 1997-244730/22  
 PA: (AMCY) AMERICAN CYANAMID CO; (IMMV) IMMUNEX CORP  
 IN: GOMBOTZ, W; HUANG, W J; LAWTER, J R; PANKEY, S;  
 PETTIT, D; LAWTER, J; GOMBOTZ, W R; PANKEY, S C;  
 PETTIT, D K  
 US 5990194 A 1990-147718/19  
 PA: (ATRI-N) ATRIX LAB INC; (DUNN-I) DUNN R L; (SOUR)  
 SOUTHERN RES INST  
 IN: COWSAR, D R; DUNN, R L; ENGLISH, J P; VANDERBILT, D P;  
 VANDERBILT, D D  
 US 5994341 A 1995-074997/10  
 PA: (ANGI-N) ANGIOGENESIS TECHNOLOGIES INC; (UYBR-N) UNIV  
 BRITISH COLUMBIA; (ANGI-N) ANGIOTECH PHARM INC;  
 (ANGI-N) ANGIOTECH PHAR INC  
 IN: ARSENAULT, A L; BURT, H M; HUNTER, W L; JACKSON, J K;  
 MACHAN, L S; ARSENAULT, L A; ARSENAULT, A  
 US 6410056 B1 EP 52510 A 1982-44213E/22  
 PA: (SYNT) SYNTAX USA INC  
 IN: KENT, J S; LEWIS, D H; SANDERS, L M; TICE, T R  
 US 3540444 A 1970-84133R/45  
 PA: (SCHB) SCHERER CORP R P  
 US 3788315 A 1974-10999V/06  
 PA: (LAUR-I) LAURENS S  
 US 4166800 A 1979-68042B/37  
 PA: (SANO) SANDOZ INC  
 IN: FONG, F W  
 US 4384975 A 1981-95485D/52  
 PA: (SANO) SANDOZ LTD  
 IN: FONG, J W  
 US 4415557 A 1982-68470E/33  
 PA: (FARB) BAYER AG  
 IN: BENZ, G; METZGER, K G; PFITZNER, J; SCHMIDT, D;  
 SCHROEDER, T; WEYLAND, H  
 US 4530840 A 1984-064255/11  
 PA: (STOL-N) STOLLE RES & DEV; (SOUR) SOUTHERN RES INST  
 IN: BECK, L R; COWSAR, D R; LEWIS, D H; TICE, T R  
 US 4542025 A 1985-248956/40  
 PA: (SOUR) SOUTHERN RES INST; (STOL-N) STOLLE RES & DEV  
 IN: BECK, L R; COWSAR, D R; LEWIS, D H; TICE, T R  
 US 4585482 A 1986-131060/20  
 PA: (SOUR) SOUTHERN RES INST  
 IN: GILLEY, R M; MEYERS, W E; SHANNON, W M; TICE, T R  
 US 4622244 A 1986-318526/48  
 PA: (UNIW) UNIV WASHINGTON  
 IN: LAPKA, G G; MASON, N S; THIES, C  
 US 4637905 A 1987-042802/06  
 PA: (BATT) BATTILLE DEV CORP  
 IN: GARDNER, D L  
 US 4675189 A 1987-192071/27  
 PA: (SYNT) SYNTAX (USA)

IN: KENT, J S; LEWIS, D H; RICE, T R; SANDERS, L M  
US 4798786 A 1989-046157/06  
PA: (STOL-N) STOLLE RES & DEV  
IN: MEYERS, W E; TICE, T R  
US 4835139 A 1987-228660/33  
PA: (DEBI-N) DEBIOPHARM SA  
IN: MAUVERNAY, R Y; ORSOLINI, P; SCHALLY, A V; TICE, T R  
US 4863735 A 1988-105413/15  
PA: (MASI) MASSACHUSETTS INST TECHNOLOGY  
IN: FOX, J G; KOHN, J B; LANGER, R S; NIEMI, S M  
US 4897268 A 1989-040741/06  
PA: (SOUR) SOUTHERN RES INST  
IN: GILLEY, R M; TICE, T R  
US 4938763 A 1990-147718/19  
PA: (ATRI-N) ATRIX LAB INC; (DUNN-I) DUNN R L; (SOUR) SOUTHERN RES INST  
IN: COWSAR, D R; DUNN, R L; ENGLISH, J P; VANDERBILT, D P; VANDERBILT, D D  
US 4941880 A 1990-245877/32  
PA: (BIOJ-N) BIOJECT INC  
IN: BURNS, M  
US 5000886 A 1988-339310/48  
PA: (AMCY) AMERICAN CYANAMID CO  
IN: LANZILOTTI, M G; LAWTER, J R  
US 5019096 A 1989-235738/33  
PA: (UYCO) UNIV COLUMBIA NEW YORK; (UYCO-N) COLUMBIA UNIV  
IN: FOX, C L; MODAK, S M; SAMPATH, L A  
US 5059187 A 1991-332380/45  
PA: (DEYL-N) DEY LABS INC;  
IN: RAFF, A M; SPERRY, C R  
US 5064413 A 1991-141962/20  
PA: (BIOJ-N) BIOJECT INC  
IN: MCKINNON, C N; NAKAGAWA, T; WILCOX, C E  
US 5075109 A 1989-272277/38  
PA: (SOUR) SOUTHERN RES INST; (UABR-N) UAB RES FOUND; (UABR-N) UAB RES FOUNDATION  
IN: ELDRIDGE, J H; GILLEY, R M; STAAS, J K; TICE, T R; STASS, J K; TICE, T T  
US 5102872 A 1992-141144/17  
PA: (CETU) CETUS CORP  
IN: GILLEY, R M; HUDSON, M E; NUNBERG, J H; SINGH, M; TAFORO, T A; TICE, T R  
US 5129825 A 1992-258764/31  
PA: (DISC-I) DISCKO J J; (DISC-I) DISCKO J  
IN: DISCKO, J J; DISCKO, J  
US 5133701 A 1990-376340/51  
PA: (HANS-I) HAN S I  
IN: HAN, S I  
US 5236355 A 1990-211295/28  
PA: (AMCY) AMERICAN CYANAMID CO  
IN: BRIZZOLARA, N S; LANZILOTTI, M G; LAWTER, J R  
US 5278202 A 1990-147718/19  
PA: (ATRI-N) ATRIX LAB INC; (DUNN-I) DUNN R L; (SOUR) SOUTHERN RES INST  
IN: COWSAR, D R; DUNN, R L; ENGLISH, J P; VANDERBILT, D P; VANDERBILT, D D  
US 5290494 A 1994-074278/09  
PA: (TEXA) UNIV TEXAS SYSTEM  
IN: BOYAN, B D; COOMBES, A G A; HECKMAN, J D  
US 5360610 A 1991-369011/50  
PA: (SOUR) SOUTHERN RES INST  
IN: DILLON, D L; MASON, D W; TICE, T R; DAHLSTROM, A B; MCRAE-MCFARLANE, A

US 5384133 A 1988-063906/09  
PA: (INNO-N) INNOVATA BIOMED LTD; (BOYE-I) BOYES R N  
IN: BOYES, R N; GILLEY, R M; PLEDGER, K L; TICE, T R  
US 5407609 A 1990-361292/48  
PA: (SOUR) SOUTHERN RES INST;  
IN: GILLEY, R M; TICE, T R  
US 5417986 A 1995-199683/26  
PA: (USSA) US SEC OF ARMY  
IN: BOEDEKER, E C; REID, R H; SETTERSTROM, J A; VAN  
HAMONT, J E  
US 5429822 A 1993-303139/38  
PA: (CAMB-N) CAMBRIDGE SCI INC  
IN: AUGENSTEIN, D C; GRESSER, J D; JIMOH, A G; KUETHE, D  
O; TRANTOLO, D J; WISE, D L  
US 5500228 A 1990-211296/28  
PA: (AMCY) AMERICAN CYANAMID CO  
IN: LANZILOTTI, M G; LAWTER, J R  
US 5538739 A 1996-353786/35  
PA: (NOVS) NOVARTIS INC; (SANO) SANDOZ LTD  
IN: BODMER, D; FONG, J W; KISSEL, T; MAULDING, H V;  
NAGELE, O; PEARSON, J E  
US 5639480 A 1997-332008/30  
PA: (NOVS) NOVARTIS INC; (SANO) SANDOZ LTD; (NOVS)  
NOVARTIS AG  
IN: BODMER, D; FONG, J W; KISSEL, T; MAULDING, H V;  
NAGELE, O; PEARSON, J E  
US 5643605 A 1995-170022/22  
PA: (GETH) GENENTECH INC  
IN: CLELAND, J L; LIM, A; POWELL, M F  
US 5648096 A 1994-167187/20  
PA: (SCHW-N) SCHWARZ PHARMA AG  
IN: GANDER, B; MERKLE, H P  
US 5650173 A 1995-200182/26  
PA: (ALKE-N) ALKERMES CONTROLLED THERAPEUTICS; (MEDI-N)  
MEDISORB TECHNOLOGIES INT LP  
IN: ATKINS, T J; HAZRATI, A M; HERBERT, P F; RAMSTACK, J  
M; STROBEL, J; RAMSTACK, M J  
US 5688530 A 1992-042911/06  
PA: (SANO) SANDOZ-ERFINDUNGEN VERW GMBH; (SANO) SANDOZ  
LTD; (SANO) SANDOZ AG; (PRIK-I) PRIKOSZOVICH W; (NOVS)  
NOVARTIS AG; (SANO) SANDOZ SA  
IN: PRIKOSZOVICH, W; PRIKOSZOVI, W; BODMER, D; FONG, J W;  
KISSEL, T; MAULDING, H V; NAGELE, O; PEARSON, J E  
US 5693343 A 1998-031704/03  
PA: (USSA) US SEC OF ARMY  
IN: BOEDEKER, E C; BROWN, W R; REID, R H; THIES, C; VAN  
HAMONT, J E  
US 5762965 A 1998-347245/30  
PA: (USSA) US SEC OF ARMY  
IN: BIRX, D L; BURNETT, P R; REID, R H; SETTERSTROM, J A;  
VAN COTT, T C; VAN HAMONT, J E  
US 5811128 A 1998-530832/45  
PA: (SOUR) SOUTHERN RES INST; (UABR-N) UAB RES FOUND  
IN: ELDRIDGE, J H; GILLEY, R M; STAAS, J K; TICE, T R  
US 5814344 A 1998-541706/46  
PA: (SOUR) SOUTHERN RES INST; (UABR-N) UAB RES FOUND  
IN: ELDRIDGE, J H; GILLEY, R M; STAAS, J K; TICE, T R  
US 5820883 A 1998-567595/48  
PA: (SOUR) SOUTHERN RES INST; (UABR-N) UAB RES FOUND  
IN: ELDRIDGE, J H; GILLEY, R M; STAAS, J K; TICE, T R  
US 5853763 A 1999-094826/08  
PA: (SOUR) SOUTHERN RES INST; (UABR-N) UAB RES FOUND  
IN: ELDRIDGE, J H; GILLEY, R M; STAAS, J K; TICE, T R

WO 9832427 A Y EP 52510 B 1982-44213E/22  
 PA: (SYNT) SYNTEX USA INC  
 IN: KENT, J S; LEWIS, D H; SANDERS, L M; TICE, T R  
 Y US 5486503 A 1996-097084/10  
 PA: (UYBO-N) UNIV BOSTON  
 IN: OPPENHEIM, F G; XU, T

REN LITERATURE CITATIONS UPR: 20030131

Citations by Examiner

CITING PATENT	CAT	CITED LITERATURE
US 6309669	B1	Yeh et al. A Novel Emulsification-Solvent extraction Technique for Production of Protein Loaded Biodegradable Microparticles for vaccine and Drug Delivery. 1995, 33(3), pp. 437-445.*
US 6309669.	B1	Wang et al. Influence of Formulation Methods on the in vitro Controlled Release of Protein from Poly(ester) Microspheres. J. of Controlled Release. Sep. 1991, vol. 17, pp. 23-31.*
US 6309669	B1	Yan et al. Characterization and Morphological Analysis of Protein-Loaded Poly(Lactide-co-Glycolide) Microparticles Prepared by WOW Emulsion Technique. J. of Con. Rel. 1994, 32(3). pp. 231-241.*
US 6309669	B1	Jeyanthi et al. Novel, Burst-Free, Programmable Biodegradable Microspheres for Controlled Release of Polypeptides. In: Proceedings International Symposium on Controlled Release of Bioactive.*
US 6309669	B1	Materials 1996. Pp. 351-352.
US 6410056	B1	Maister, First Oral AIDS Vaccine Trials Near, BioWorld Today, Tuesday, Apr. 19, 1994, p. 4.
US 6410056	B1	Wang, et al., Influence of formulation methods on the in vitro controlled release of protein from poly (ester) microspheres Journal of Controlled Release, 17 (1991) 23-32.
US 6410056	B1	Brown, Wonder Drugs' Losing Healing Aura, The Washing Post, Jun. 26, 1995, A section.
US 6410056	B1	Rognan, et al., Molecular Modeling of an Antigenic Complex Between a Viral Peptide and a Class I Major Histocompatibility Glycoprotein, Proteins Structure, Function and Genetics 13 70-85 (1992).
US 6410056	B1	Brown, A hypothetical model of the foreign antigen binding site of Class II histocompatibility molecules, Nature, vol. 332, Apr. 28 1988, pp. 845-850.
US 6410056	B1	Jeyanthi, et al., Novel, Burst Free Programmable Biodegradable Microspheres For Controlled Release of Polypeptides, Proceedings Int. Symp. control Release Bioact. Mater. (1996) pp. 351-352/.
US 6410056	B1	Yeh, A novel emulsification-solvent extraction technique for production of protein loaded biodegradable microparticles for vaccine and drug delivery, Journal of Controlled Release, 33 (1005) 437-445.
US 6410056	B1	Yan, Characterization and morphological analysis of protein-loaded poly(lactide-co-glycolide) microparticles prepared by water-in-oil-in-water emulsion technique, Journal of Controlled Release, 32 (1994) 231-241.

- US 6410056 B1 Gilding, Biodegradable polymers for use in surgery-polyglycolic/poly (ac c acid) homo-and copolymers: 1, Polymer, vol. 20, Dec. 1979, pp. 1459-1464.
- US 6410056 B1 Biotechnology News, Aug. 22, 1997, vol. 17, No. 20, Topical DNA vaccine elicits immune response.
- US 6410056 B1 Hall, et al., Purification and Analysis of Colonization Factor Antigen I, Coli Surface Antigen 1, and Coli Surface ANTigen 3 Fimbriae from Enterotoxigenic Escherichia Coli, Journal of Bacteriology, Nov. 1989, pp. 6372-6374, vol. 171, No. 11.
- US 6410056 B1 Evans, et al. Purification and Characterization of the CFR/I Antigen of Enterotoxigenic Escherichia coli, Infection and Immunity, Aug. 1979, pp. 738-748, vol. 25.
- US 6410056 B1 Karjalainen, et al., Molecular Cloning and Nucleotide Sequence of the Colonization Factor Antigen I Gene of Escherichia coli, Infection and Immunity, Apr. 1989, pp. 1126-1130, vol. 57.
- US 6410056 B1 Jordi, et al., Analysis of the first two genes of the CS1 fimbrial operon in human enterotoxigenic Escherichia coli of serotype O139: H28, FEMS Microbiology Letters 80, (1991) pp. 265-270.
- US 6410056 B1 Tan, et al., Mapping the Antigenic Epitopes of Human Dihydrofolate Reductase by Systematic Synthesis of Peptides on solid Supports, The Journal of Biological Chemistry, vol. 265, No. 14, Issue of May 15, pp. 8022-8026 (1990).
- US 6410056 B1 McConnel, et al., Antigenic homology within human enterotoxigenic Escherichia coli fimbrial colonization factor antigens: CFA/I, coli-surface-associated antigens (CS)1, CS2, CS4 and CS17, FEMS Microbiology Letters 61 (1989) 105-108.
- US 6410056 B1 Van der Zee, Efficient mapping and characterization of a T cell epitope by the simultaneous synthesis of multiple peptides, Eur. J. Immunol. 1989, 19: 43-47.
- US 6410056 B1 Cassels, et al., Analysis of Escherichia coli Colonization Factor Antigen I Linear B-Cell Epitopes, as Determined by Primate Responses, following Protein Sequence Verification, Infection and Immunity, Jun. 1992, pp. 2174-2181, vol. 60, No. 6.
- US 6410056 B1 Setterstrom, Controlled Release of Antibiotics From biodegradable Microcapsules For Wound infection Control, Chemical Abstracts, 1983, pp. 215-226.
- US 6410056 B1 Perez-Casal, et al., Gene Encoding the Major Subunit of CS1 Pili of Human Enterotoxigenic Escherichia Coli, Infection and Immunity, Nov., 1990, pp. 3594-3600, vol. 58, No. 11.
- US 6410056 B1 Romagnoli, et al. Peptide-MHC Interaction: A Rational Approach to Vaccine Design, Inter, RE. Immunol. 6, 1990, 00 61-73.
- WO 9832427 A YEH et al., "A Novel Emulsification-Solvent Extraction Technique for Production of Protein Loaded Biodegradable Microparticles for Vaccine and Drug Delivery", 1995, Vol. 33, No. 3, pages 437-445.
- WO 9832427 A PROCEEDINGS INTERNATIONAL SYMPOSIUM ON CONTROLLED RELEASE OF BIOACTIVE MATERIALS, 1996, JEYANTHI et

- al., "Novel, Burst-Free, Programmable Biodegradable Microspheres for Controlled Release of Polypeptides", pages 351-352, XP002914204
- WO 9832427 A J. OF CONTROLLED RELEASE, 1994, Vol. 32, No. 3, YAN et al., "Characterization and Morphological Analysis of Protein-Loaded Poly(Lactide-co-Glycolide) Microparticles Prepared by Water-in-Oil-in-Water Emulsion Technique", pages 231-241, XP002914206
- WO 9832427 A YEH et al., "A Novel Emulsification-Solvent Extraction Technique for Production of Protein Loaded Biodegradable Microparticles for Vaccine and Drug Delivery", 1995, Vol. 33, No. 3, pages 437-445, XP002914207
- WO 9832427 A J. OF CONTROLLED RELEASE, September 1991, Vol. 17, WANG et al., "Influence of Formulation Methods on the In Vitro Controlled Release of Protein from Poly(ester) Microspheres", pages 23-31, XP002914205
- WO 9832427 A PROCEEDINGS INTERNATIONAL SYMPOSIUM ON CONTROLLED RELEASE OF BIOACTIVE MATERIALS, 1996, JEYANTHI et al., "Novel, Burst-Free, Programmable Biodegradable Microspheres for Controlled Release of Polypeptides", pages 351-352.
- WO 9832427 A J. OF CONTROLLED RELEASE, September 1991, Vol. 17, WANG et al., "Influence of Formulation Methods on the In Vitro Controlled Release of Protein from Poly(ester) Microspheres", pages 23-31.
- WO 9832427 A J. OF CONTROLLED RELEASE, 1994, Vol. 32, No. 3, YAN et al., "Characterization and Morphological Analysis of Protein-Loaded Poly(Lactide-co-Glycolide) Microparticles Prepared by Water-in-Oil-in-Water Emulsion Technique", pages 231-241.

CGP CITING PATENTS

UPG: 20031208

Cited by Examiner

CITED PATENT	CAT	CITING PATENT	ACCNO
US 6309669	B1	US 6576226	B1 2003-605494/52
	PA:	(JERN-I) JERNBERG G R	
	IN:	JERNBERG, G R	
WO 9832427	A A	WO 200050014	A2 2000-587126/52
	PA:	(MYLA-N) MYLAN PHARM INC	
	IN:	ADDICKS, W J; BENSON, K R; DUDA, J P; SNIDER, D A	
WO 9832427	Al	DE 19850445	Al 2000-330249/22
	PA:	(FALK-N) FALK PHARMA GMBH	
	IN:	KIST, M; OTTERBECK, N	
		DE 19916384	Al 2000-673556/62
	PA:	(SCHD) SCHERING AG	
	IN:	ALBAYRAK, C; HOFFMANN, K; TACK, J	
		GB 2354438	A 2001-427248/42
	PA:	(PROC) PROCTER & GAMBLE CO	
	IN:	JAMES, M I; NARINX, E; SPEDER, A E M; STODDART, B; STONEHOUSE, J R	
		US 6274168	B1 2000-587126/52
	PA:	(MYLA-N) MYLAN PHARM INC	
	IN:	ADDICKS, W J; BENSON, K R; DUDA, J P; SNIDER, D A	
		US 6620432	B2 2002-154070/22

PA: (MYLA-N) MYLAN PHARM INC  
 IN: ADDICKS, W J; BENSON, K R; DUDA, J P; SNIDER, D A

L142 ANSWER 5 OF 6 DPCI COPYRIGHT 2004 THOMSON DERWENT on STN  
 AN 1998-347245 [30] DPCI  
 CR 1991-295351 [40]; 1992-398530 [48]; 1995-199683 [26]; 1996-019737 [02];  
 1997-393337 [36]; 1998-031704 [03]; 1998-129287 [12]; 1998-437043 [37];  
 2001-396353 [42]; 2003-101718 [09]; 2003-615263 [58]; 2003-730043 [69];  
 2003-730422 [69]  
 DNN N1998-271056 DNC C1998-107209  
 TI Vaccine compositions containing antigens in microspheres - useful for  
 augmenting immune reactions across mucosal surfaces, especially against  
 HIV-1.  
 DC A23 A96 B04 D16 P32  
 IN BIRX, D L; BURNETT, P R; REID, R H; SETTERSTROM, J A; VAN COTT, T C; VAN  
 HAMONT, J E  
 PA (USSA) US SEC OF ARMY  
 CYC 1  
 PI US 5762965 A 19980609 (199830)\* 6p A61K009-00  
 ADT US 5762965 A Cont of US 1984-590308 19840316, CIP of US 1990-521945  
 19900511, CIP of US 1991-690485 19910424, CIP of US 1991-805721 19911121,  
 CIP of US 1992-867301 19920410, CIP of US 1994-242960 19940516, CIP  
 of US 1995-446149 19950522, US 1996-598874 19960209  
 FDT US 5762965 A CIP of US 5417986  
 PRAI US 1996-598874 19960209; US 1984-590308 19840316; US 1990-521945  
 19900511; US 1991-690485 19910424; US 1991-805721 19911121; US  
 1992-867301 19920410; US 1994-242960 19940516; US 1995-446149  
 19950522  
 IC ICM A61K009-00  
 ICS A61F013-00; A61K009-14; A61K009-66  
 FS CPI GMPI

EXF EXAMINER'S FIELD OF SEARCH UPE: 19980803  
 -----

NCL US 5762965 A 19980609  
 424/422; 424/426; 424/455; 424/486; 424/488; 424/499

# CTCS CITATION COUNTERS

PNC.DI	0	Cited Patents Count (by inventor)
PNC.DX	2	Cited Patents Count (by examiner)
IAC.DI	0	Cited Issuing Authority Count (by inventor)
IAC.DX	1	Cited Issuing Authority Count (by examiner)
PNC.GI	0	Citing Patents Count (by inventor)
PNC.GX	5	Citing Patents Count (by examiner)
IAC.GI	0	Citing Issuing Authority Count (by inventor)
IAC.GX	1	Citing Issuing Authority Count (by examiner)
CRC.I	0	Cited Literature References Count (by inventor)
CRC.X	0	Cited Literature References Count (by examiner)

CDP CITED PATENTS UPD: 19980803  
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Cited by Examiner  
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CITING PATENT	CAT	CITED PATENT	ACCNO
US 5762965	A	US 4863735	A 1988-105413/15
PA: (MASI) MASSACHUSETTS INST TECHNOLOGY			

IN: FOX, J G; KOHN, J B; LANGER, R S; NIEMI, S M  
 US 4897268 A 1989-040741/06  
 PA: (SOUR) SOUTHERN RES INST  
 IN: GILLEY, R M; TICE, T R

CGP CITING PATENTS

UPG: 20031115

Cited by Examiner

CITED PATENT	CAT	CITING PATENT	ACCNO
US 5762965	A	US 6217911	B1 2001-396353/42
PA: (USSA) US SEC OF ARMY			
IN: SETTERSTROM, J A; VAN HAMONT, J E; VAUGHN, W M		US 6410056	B1 1998-437043/31
PA: (USSA) US SEC OF ARMY			
IN: BOEDEKER, E C; FRIDEN, P; JACOB, E; JEYANTHI, R; MCQUEEN, C E; REID, R H; ROBERTS, F D; SETTERSTROM, J A; TICE, T R; VAN HAMONT, J E; BROWN, W; CASSELS, F; JARBOE, D L; THIES, C		US 6447796	B1 2003-101718/02
PA: (USSA) US SEC OF ARMY			
IN: DUONG, H; JACOB, E; SETTERSTROM, J A; VAN HAMONT, J; VAUGHAN, W; VOOK, N C		US 6528097	B1 2003-615263/52
PA: (USSA) US SEC OF ARMY			
IN: SETTERSTROM, J A; VAN HAMONT, J E; VAUGHN, W M		US 6596278	B2 1995-240449/31
PA: (GFFF-N) GFF GES FOERDERUNG IND ORIENTIERTEN FORS; (GFFF-N) GFF GES FOERDERUNG INDUSTRIEORIENTIERTEN; (CORR-I) CORRADIN G; (GAND-I) GANDER B; (MENY-I) MEN Y; (MERK-I) MERKLE H P; (THOM-I) THOMASIN C; (RMFD-N) RMF DICTAGENE SA			
IN: CORRADIN, G; GANDER, B; MEN, Y; MERKLE, H P; THOMASIN, C			

L142 ANSWER 6 OF 6 DPCI COPYRIGHT 2004 THOMSON DERWENT on STN

AN 1997-393337 [36] DPCI  
 CR 1991-295351 [40]; 1995-199683 [26]; 1996-019737 [02]; 1998-031704 [03]; 1998-129287 [12]; 1998-347245 [30]; 1998-437043 [37]; 2001-396353 [42]; 2003-101718 [09]; 2003-615263 [58]; 2003-730043 [69]; 2003-730422 [69]  
 DNC C1997-126303  
 TI Microcapsule compositions for burst-free, sustained release of active agents - comprising active agent and blend of uncapped and end-capped biodegradable poly(lactide/glycolide).  
 DC A23 A25 A96 B04 B07  
 IN FRIDEN, P; JEYANTHI, R; MCQUEEN, C E; REID, R H; ROBERTS, F D; SETTERSTROM, J A; VAN HAMONT, J F  
 PA (USSA) US SEC OF ARMY  
 CYC 71  
 PI WO 9726869 A1 19970731 (199736)\* EN 52p A61K009-50 <--  
 RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MN NL OA PT SD  
 SE SZ UG  
 W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS  
 JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT  
 RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN  
 AU 9714104 A 19970820 (199749)  
 EP 817619 A1 19980114 (199807) EN  
 R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE  
 NZ 325561 A 19990629 (199931) A61K009-50  
 JP 11509862 W 19990831 (199946) 40p A61K009-52



KR 98703429 A 19981105 (199954)  
 MX 9707310 A1 19980601 (200009)  
 BR 9607752 A 19991130 (200014)  
 AU 722884 B 20000810 (200043)  
 NZ 335409 A 20001222 (200104) A61K009-52  
 CN 1188408 A 19980722 (200270) A61K009-50  
 ADT WO 9726869 A1 WO 1996-US19440 19961118; AU 9714104 A AU 1997-14104  
 19961118; EP 817619 A1 EP 1996-944247 19961118, WO 1996-US19440 19961118;  
 NZ 325561 A NZ 1996-325561 19961118, WO 1996-US19354 19961118; JP 11509862  
 W WO 1996-US19440 19961118, JP 1997-526833 19961118; KR 98703429 A WO  
 1996-US19440 19961118, KR 1997-706833 19970924; MX 9707310 A1 MX 1997-7310  
 19970924; BR 9607752 A BR 1996-7752 19961118, WO 1996-US19440 19961118; AU  
 722884 B AU 1997-14104 19961118; NZ 335409 A Div ex NZ 1996-325561  
 19961118, NZ 1996-335409 19961118; CN 1188408 A CN 1996-194768 19961118  
 FDT AU 9714104 A Based on WO 9726869; EP 817619 A1 Based on WO 9726869; NZ  
 325561 A Based on WO 9726869; JP 11509862 W Based on WO 9726869; KR  
 98703429 A Based on WO 9726869; BR 9607752 A Based on WO 9726869; AU  
 722884 B Previous Publ. AU 9714104, Based on WO 9726869; NZ 335409 A Div  
 ex NZ 325561  
 PRAI US 1996-590973 19960124  
 IC ICM A61K009-50; A61K009-52  
 ICS A61K038-08; A61K038-09; A61K038-10; A61K047-30  
 FS CPI

## CTCS CITATION COUNTERS

PNC.DI	0	Cited Patents Count (by inventor)
PNC.DX	9	Cited Patents Count (by examiner)
IAC.DI	0	Cited Issuing Authority Count (by inventor)
IAC.DX	4	Cited Issuing Authority Count (by examiner)
PNC.GI	0	Citing Patents Count (by inventor)
PNC.GX	1	Citing Patents Count (by examiner)
IAC.GI	0	Citing Issuing Authority Count (by inventor)
IAC.GX	1	Citing Issuing Authority Count (by examiner)
CRC.I	0	Cited Literature References Count (by inventor)
CRC.X	4	Cited Literature References Count (by examiner)

CDP CITED PATENTS UPD: 19991105

## Cited by Examiner

CITING PATENT	CAT	CITED PATENT	ACCNO
EP 817619	A A	DE 4005415	A 1991-253598/35
PA:		(BOEH) BOEHRINGER INGELHEIM; (BOEH) BOEHRINGER INGELHEIM KG; (BOEH) BOEHRINGER INGELHEIM INT GMBH; (BOEH) BOEHRINGER INGELHEIM GMBH	
IN:		BUCHHOLZ, B	
A		DE 4235312	A 1993-145015/18
PA:		(BOEH) BOEHRINGER INGELHEIM KG; (BOEH) BOEHRINGER INGELHEIM INT GMBH; (BOEH) BOEHRINGER INGELHEIM GMBH	
IN:		BUCHHOLZ, B; ENTENMANN, G	
A		DE 19513659	A 1996-413621/42
PA:		(BOEF) BOEHRINGER MANNHEIM GMBH;	
IN:		KISSEL, T; KOLL, H; MORLOCK, M; WINTER, G	
A		EP 52510	A 1982-44213E/22
PA:		(SYNT) SYNTAX USA INC	
IN:		KENT, J S; LEWIS, D H; SANDERS, L M; TICE, T R	
A		EP 463194	A 1992-008949/02

PA: (BOEH) BOEHRINGER INGELHEIM; (BOEH) BOEHRINGER  
 INGELHEIM GMBH  
 IN: BENDIX, D; STRICKER, H  
 A US 5410016 A 1995-205596/27  
 PA: (TEXA) UNIV TEXAS SYSTEM  
 IN: DESAI, N P; HILL, J L; HUBBELL, J A; PATHAK, C P;  
 SAWHNEY, A S  
 WO 9726869 A 1997-393337/36  
 PA: (USSA) US SEC OF ARMY  
 IN: FRIDEN, P; JEYANTHI, R; MCQUEEN, C E; REID, R H;  
 ROBERTS, F D; SETTERSTROM, J A; VAN, HAMONT J F  
 WO 9726869 A A US 4622244 A 1986-318526/48  
 PA: (UNIW) UNIV WASHINGTON  
 IN: LAPKA, G G; MASON, N S; THIES, C  
 A US 4623588 A 1986-325607/49  
 PA: (BIOT-N) BIOTEK INC  
 IN: NUCEFORA, W A; NUWAYSER, E S

REN LITERATURE CITATIONS UPR: 19991105

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 Citations by Examiner  
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CITING PATENT	CAT	CITED LITERATURE
EP 817619	A	See references of WOA 9726869
EP 817619	A	R. JEYANTHI ET AL.: "NOVEL BURST FREE PROGRAMMABLE BIODEGRADABLE MICROSPHERES FOR CONTROLLED RELEASE OF POLYPEPTIDES" PROC. INT. SYMP. CONTROL. RELEASE BIOACT. MATER. (1996), July 1996, pages 351-352, XP002086331 KYOTO
EP 817619	A	See also references of WOA 9726869
WO 9726869	A	See also references of EPA 0817619

CGP CITING PATENTS UPG: 20010612

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CITED PATENT	CAT	CITING PATENT	ACCNO
WO 9726869	A1	US 6217893	B1 1998-609923/51
		PA: (PHAR-N) PHARMA BIOTECH; (PHAR-N) PHARMA BIOTECH SA	
		IN: PELLET, M; ROUME, C	

=> d his

(FILE 'HOME' ENTERED AT 09:25:38 ON 09 FEB 2004)  
 SET COST OFF

FILE 'REGISTRY' ENTERED AT 09:26:33 ON 09 FEB 2004  
 E METHYLENE CHLORIDE/CN

L1 1 S E3  
 L2 15 S 189943-94-0 OR 153439-97-5 OR 146447-66-7 OR 142227-56-3 OR 1  
 L3 448 S (C2H4O3 OR C4H4O4) AND (C3H6O3 OR C6H8O4)  
 L4 26 S L3 AND 2/NC  
 L5 11 S L4 NOT L2  
 L6 4 S 10326-41-7 OR 79-33-4 OR 50-21-5 OR 26100-51-6  
 L7 10 S 22098-76-6 OR 13076-19-2 OR 13076-17-0 OR 4511-42-6 OR 95-96-  
 L8 5 S 26009-03-0 OR 502-97-6 OR 79-14-1 OR 26202-08-4 OR 26124-68-5

E (C5H6O4)N/MF  
 13 S E3

L9

FILE 'HCAPLUS' ENTERED AT 09:42:24 ON 09 FEB 2004

L10 23379 S L1  
 L11 13139 S METHYLENE CHLORIDE OR METHYLENECHLORIDE  
 L12 19 S METHANECHLORIDE OR METHANE CHLORIDE  
 L13 19407 S DICHLOROMETHANE OR (DICHLORO OR DI CHLORO)()METHANE OR AEROTH  
 L14 37830 S L10-L13  
 L15 4318 S L2  
 L16 57214 S L6,L7  
 L17 136893 S LACTIC ACID OR LACTATE OR (POLYLACTIC OR POLY LACTIC)()ACID O  
 L18 10124 S L8  
 L19 18332 S GLYCOLIC ACID OR GLYCOLATE OR (POLYGLYCOLIC OR POLY GLYCOLIC)  
 L20 7048 S L16,L17 AND L18,L19  
 L21 274 S L15 AND L14  
 L22 186 S L20 AND L14  
 L23 318 S L21,L22  
 L24 2273 S (POLYLACTIDE OR POLY(L)LACTIDE) AND (POLYGLYCOLIDE OR POLY(L)  
 L25 8801 S (POLYLACTIDE OR POLY(L)LACTIDE OR L16,L17) AND (POLYGLYCOLIDE  
 L26 283 S L14 AND L24,L25  
 L27 323 S L23,L26  
 L28 10266 S (?LACTIC? OR ?LACTIDE? OR ?LACTATE? OR L16 OR L17) AND (?GLY  
 L29 318 S L28 AND L14  
 L30 329 S L27,L29  
 L31 5 S L30 AND (ENDCAP? OR END CAP? OR UNCAP?)  
 L32 97 S L30 AND CONTROL?(L)RELEAS?  
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 L34 1 S L33 AND L31  
 L35 18 S L32 AND L33  
 L36 19 S L34,L35  
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 L37 3 S E4,E5  
 E VAN HAMONT J/AU  
 L38 25 S E3-E8  
 E REID R/AU  
 L39 92 S E3,E15-E17  
 E REID ROBERT/AU  
 L40 76 S E1,E3,E16-E20  
 E JACOB E/AU  
 L41 81 S E3-E11  
 L42 12 S E18,E19  
 E JEYANTHI R/AU  
 L43 22 S E3,E4  
 E BOEDEKER E/AU  
 L44 65 S E3,E4,E6,E7  
 E MCQUEEN C/AU  
 L45 22 S E3,E5,E10,E11  
 E JARBOE D/AU  
 L46 8 S E5,E6,E7  
 E CASSELS F/AU  
 L47 45 S E3-E9  
 E BROWN W/AU  
 L48 1836 S E3-E70  
 E BROWN WIL/AU  
 L49 5 S E12-E16  
 L50 1 S E22  
 L51 835 S BROWN WILLIAM?/AU  
 E THIES C/AU  
 L52 108 S E3-E5,E11  
 E TICE T/AU  
 L53 80 S E3,E4,E6-E9  
 E ROBERTS F/AU

L54 55 S E3,E8,E9  
 L55 11 S E44-E47,E29  
 L56 1 S E55  
 L57 1 S E67  
 L58 1 S E83  
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 L59 62 S E3-E10  
 E SETTERSTROM J/AU  
 L60 30 S E3-E6  
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 L68 0 S L33 AND E83,E84  
 L69 0 S L33 AND E89  
 L70 1 S L33 AND E97,E107,E108  
 L71 1 S L33 AND E112,E113,E115,E116  
 L72 0 S L33 AND E123,E128  
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 L74 0 S L33 AND E148,E150  
 L75 1 S L33 AND E162  
 L76 1 S L33 AND E182,E187,E188  
 L77 0 S L33 AND E195,E196,E199,E200,E201,E203  
 L78 0 S L33 AND E209,E211,E212  
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 L81 1 S L33 AND E40,E46,E47  
 L82 0 S L33 AND E51,E53,E56,E59  
 L83 1 S L33 AND E62,E63,E68,E69  
 L84 0 S L33 AND E81  
 L85 0 S L33 AND E83,E87,E96  
 L86 5 S L33 AND E105,E106  
 L87 9 S L33 AND E110,E111,E113,E114  
 L88 0 S L33 AND E121,E131,E132  
 L89 0 S L33 AND E134,E135,E136,E144  
 L90 1 S L33 AND E146  
 L91 4 S L33 AND E158  
 L92 0 S L33 AND E179  
 L93 9 S L33 AND E184,E185,E192  
 L94 0 S L33 AND E193,E196,E197,E198,E200  
 L95 0 S L33 AND E206,E208,E209  
 L96 26 S L67-L95  
 L97 30 S L36,L96  
 L98 220 S CFA() (1 OR I)  
 L99 0 S L33 AND L98  
 L100 135 S (COLONIZ? OR COLONIS?) () FACTOR() ANTIGEN? () (1 OR 1)  
 L101 0 S L100 AND L33  
 L102 1 S COLI AND L33  
 L103 1 S (ESCHER? OR "E") () COLI AND L33  
 L104 1 S L102,L103 AND L97  
 L105 7 S L33 AND (VACCIN? OR ADJUVANT?)  
 L106 3 S L97 AND L105  
 L107 6 S L64,L104,L106  
 L108 4 S L105 NOT L107  
 L109 10 S L107,L108  
 L110 24 S L97 NOT L109  
 L111 1 S L110 AND (VACCIN? OR ADJUVANT? OR IMMUNIZ? OR IMMUNIS?)

L112 11 S L109,L111  
L113 23 S L110 NOT L112

FILE 'HCAPLUS' ENTERED AT 10:41:32 ON 09 FEB 2004

L114 11 S L112 AND L10-L113  
L115 23 S L113 AND L10-L114

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FILE 'WPIX' ENTERED AT 10:44:57 ON 09 FEB 2004

L116 33251 S (?LACTIC? OR ?LACTIDE? OR ?LACTATE?)/BIX  
E LACTIC ACID/DCN

E E3+ALL  
L117 6624 S E2 OR 0009/DRN  
E LACTIC ACID/DCN  
E E21+ALL

L118 64 S E2

L119 116 S E4

L120 7 S E6

L121 97 S E8

L122 114 S E10

L123 35091 S L17/BIX OR L116-L122

L124 9181 S (?GLYCOLIC? OR ?GLYCOLIDE? OR ?GLYCOLATE?)/BIX  
E GLYCOLIC ACID/DCN  
E E3+ALL

L125 2349 S E2 OR 0448/DRN

L126 101 S E10

L127 5254 S L19/BIX

L128 4652 S L123 AND L124-L127

L129 25928 S L11/BIX OR L12/BIX OR L13/BIX OR CH2CL2/BIX  
E METHYLENE CHLORIDE/DCN  
E E3+ALL

L130 6724 S E2 OR 0345/DRN

L131 318 S L128 AND L129,L130

L132 208 S L131 AND A61K009/IC,ICM,ICS,ICA,ICI

L133 9 S L131 AND A61K009-58/IC,ICM,ICS,ICA,ICI

L134 155 S L131 AND (B12-M11E OR C12-M11E OR B12-M10 OR C12-M10 OR B12-M

L135 135 S L131 AND (R051 OR R052)/M0,M1,M2,M3,M4,M5,M6

L136 118 S L131 AND (A61K009-48 OR A61K009-50 OR A61K009-51 OR A61K009-5

L137 3 S L133-L136 AND (ENDCAP? OR END CAP? OR UNCAP?)/BIX

L138 20 S L98/BIX OR L100/BIX

L139 0 S L133-L136 AND L138

FILE 'WPIX' ENTERED AT 10:59:26 ON 09 FEB 2004

FILE 'DPCI' ENTERED AT 11:04:35 ON 09 FEB 2004

L140 2 S (W09832427 OR W09726869 OR US65280978)/PN  
E US95-446149/AP,PRN

L141 5 S E3

L142 6 S L140 OR L141

FILE 'DPCI' ENTERED AT 11:05:40 ON 09 FEB 2004

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